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The prevalence of hepatitis C among healthcare workers: a systematic review and meta-analysis

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ABSTRACT

The aim of this study was to estimate the prevalence of viral hepatitis C (HCV) infection among healthcare workers (HCWs) compared to the general population. A systematic search for the years 1989–2014 was conducted in the Medline, Embase and Cochrane databases. Studies on hepatitis C in HCWs were included if they incorporated either a control group or reference data for the general population. The study quality was classified as high, moderate or low. Pooled effect estimates were calculated to determine the odds of occupational infection. Heterogeneity between studies was analysed using the χ^2 test ($p < 0.10$) and quantified using the I^2 test. 57 studies met our criteria for inclusion and 44 were included in the meta-analysis. Analysis of high and moderate quality studies showed a significantly increased OR for HCV infection in HCWs relative to control populations, with a value of 1.6 (95% CI 1.03 to 2.42). Stratification by study region gave an OR of 2.1 in low prevalence countries; while stratification by occupational groups gave an increased prevalence for medical (OR 2.2) and for laboratory staff (OR 2.2). The OR for professionals at high risk of blood contact was 2.7. The pooled analysis indicates that the prevalence of infection is significantly higher in HCWs than in the general population. The highest prevalence was observed among medical and laboratory staff. Prospective studies that focus on HCW-specific activity and personal risk factors for HCV infection are needed.

INTRODUCTION

Viral hepatitis C (HCV) infection is caused by blood contact and is a public health problem throughout the world. Its clinical course may be severe and can lead to work disability or to death. Considerable costs are incurred for prophylactic and treatment measures and result from the chronic clinical progress of the disease, loss of working hours and premature death. According to the WHO, approximately 150 million people in the world are chronically infected with HCV, and hepatitis C is the cause of 350 000 deaths annually.¹ HCV is mainly transmitted by contact with infected blood due to injuries to the skin or mucous membranes.² Acute infection is often asymptomatic and therefore frequently overlooked. In up to 80% of patients, the clinical course is chronic, leading to an increased risk of developing hepatic cirrhosis or hepatic cell carcinoma.³ Risk factors for HCV infection include intravenous drug consumption, injury-prone sex (men with men) and blood transfusions before the introduction of diagnostic testing. There is no vaccine or postexposure prophylaxis for HCV infection.

Healthcare workers (HCWs) have contact with infected patients and their body fluids. A particularly important factor is repeated performance of exposure prone procedures (EPPs) that may cause injuries to employees.⁴ Injuries to medical and health staff from sharp or pointed objects are among the most frequently reported occupational accidents in healthcare.⁵ The results of epidemiological studies indicate that approximately 80% of HCWs have been affected by needlestick injuries (NSI).⁶ Many such injuries go unreported.^{6–8} The risk of seroconversion after an injury depends on factors including the type of injury (deep cuts or pricks), the quantity of infectious material transferred, the virus load in the index patient and possibly genetic factors in the injured person.^{8–10}

The probability of HCV seroconversion after a NSI in Europe has been estimated as 0.42%.^{6, 8} Although HCV infection as an occupational disease is statistically rare, the consequences for the HCW and the health system are considerable.^{7, 11, 12} In 2012, 79 HCV infections were reported to the German Institution for Statutory Accident Insurance and Prevention in Health and Welfare Services, and 47 infections were recognised as occupational diseases.¹³ Numerous studies have investigated the prevalence of HCV in HCWs, but the results have been inconsistent. The objective of the present study is to estimate the prevalence of HCV infection among HCWs compared to the general population. Which professionals are particularly affected by infection?

METHODS

This study is reported in line with the Proposal for Reporting of Meta-analyses of Observational Studies (MOOSE).¹⁴

Search strategy and screening

A systematic literature search was performed in the Medline, Embase and Cochrane databases for the period from 1989 to 2014. This included all prevalence and incidence studies on hepatitis C in HCWs with either a control group or reference data on the general population. The Embase search was performed using the following search terms: (((('hepatitis C') AND 'occupational exposure') AND 'healthcare worker') AND prevalence) OR incidence)—with and without truncation (see online supplementary file). The search strategy was adapted for the other databases. Additionally, we searched reference lists of the chosen studies and prior reviews. Where it was not possible to make a decision on a study's inclusion or exclusion based on the abstract, the full text of the study was



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examined. The studies were screened and their quality was assessed by two reviewers working independently and using pre-defined checklists. Disagreements were resolved by consensus.

Studies meeting the following criteria were considered for inclusion:

- ▶ Population: HCWs in direct contact with patients or blood
- ▶ Exposure: Study examines occupational exposure
- ▶ Control: Control group/reference data for general population from other publications
- ▶ Outcome: Serological test for HCV
- ▶ Design: Prevalence and incidence studies
- ▶ Languages: German, English, French, Spanish, Portuguese, Italian.

The following criteria led to exclusion from this study:

- ▶ Population: HCWs without direct contact with patients or blood
- ▶ Exposure: No occupational exposure
- ▶ Control: No control group; reference data for the general population not taken from other publications
- ▶ Outcome: No serological test for HCV
- ▶ Design: Case reports, surveillance data.

In studies with several control groups, the ones selected were those that best reflected the general population. Studies that examined HCWs without a control group were only included when the results were compared with a population-based study performed within a period of 2 years before or after the actual investigation and in a comparable study region.

In this report, 'healthcare worker' (HCW) is defined as any person (eg, an employee or student) whose activities involve contact with patients or with blood or other body fluids from patients in a healthcare setting.¹⁵

Study quality

In accordance with the literature, we developed an instrument to assess the methodological quality of the observational studies included.^{16–20} Scores were awarded on the basis of the criteria below. A total of nine scores was possible (table 1).

Quality of the laboratory test: Anti-HCV detection depends on the type of test used, and tests differ in quality (product and procedure). In order to standardise the quality assessment, we evaluated the presence of a confirmatory test, but not its quality or procedure. It was not possible to evaluate this in the primary studies, due to missing data.

Statistical analysis

For the meta-analysis, data were extracted from the studies using a standardised documentation form. The parameters were

the number of employees examined and the proportion of employees tested as serologically positive. Prevalence ratios (ORs) were calculated as effect estimates using the Mantel-Haenszel method for dichotomous outcomes. The 95% CIs were generated. Additional analyses were performed after stratification by type of controls, study region, publication period, gender and professional group. Meta-analyses were carried out using Review Manager 5.2.

In accordance with the criteria of Trevisan *et al*,⁵⁰ a pooled analysis was performed for professionals exposed to a high risk of blood contact from EPPs. This analysis included the following professions/working areas: surgeons, midwives, microbiologists, pathologists, blood bank and dialysis staff.

Stratification by study region was performed on the basis of national prevalence rates. Based on the publications of Te and Jensen,³ Hahne *et al*²¹ and Mohd Hanafiah *et al*,²² pooled effect estimates were calculated for low prevalence countries taking into account countries of north-west Europe and the USA. Studies from Japan were analysed separately as there have been reports that the rate of seroconversion is higher in Japan than in Europe.⁸

Studies that observed no HCV infection in either group were excluded from the meta-analysis as no information about the relative probability of the event could be derived.¹⁸

Heterogeneity and sensitivity analysis

The presence of heterogeneity was tested using the χ^2 test, taking $p < 0.10$ as the level of significance. An I^2 test was performed to quantify the diversity between studies. If there was no evidence of heterogeneity, we used a variance approach with a fixed effect model.¹⁸ In cases of statistically significant heterogeneity (χ^2 p value < 0.10) and $I^2 > 50\%$, the pooled effect estimate was determined using the random effect model. To identify sources of variation, further stratification was performed relative to study quality and to performance of confirmatory tests. In addition, for the sensitivity analyses, the stability of the pooled estimate with respect to each study was investigated by excluding individual studies from the analysis.

Publication bias

Possible publication bias was visualised with a funnel plot. In addition, the probability of publication bias was tested using Egger's linear regression in SPSS V20.²³ The level of significance for asymmetry was taken as $p < 0.1$. The calculated intercept is given with a 90% confidence range.

RESULTS

A total of 3016 publications were identified in the databases and 41 by manual search. After checking for duplicates, the titles and abstracts of 954 studies were screened, leading to the exclusion of 801 studies. The full texts of 153 studies were scrutinised and 57 studies were included in the systematic review. This selection process is given in figure 1.

Table 2 gives an overview of the studies included. A total of 27 studies from Europe were included, along with 13 from Asia, eight from Africa, seven from North America and two from South America. In most studies, HCWs were examined within the inter-professional framework. In five studies, the HCWs were stratified by professional group and, in five studies, by working area or exposure. Ten studies examined only a single professional group.

In 33 out of 57 studies, population-based controls, consisting mainly of blood donors, were used. A hospital control group was used in 18 studies. Ciorlia and Zanetta³⁸ used a population-

Table 1 Checklist for quality assessment

Item	Criterion	Content	Score
1	Aim	A clearly stated aim	1
2	Sample size	>50 persons	1
3	Response rate	>50%	1
4	Length of employment	Information is available	1
5	Control group	A control group was tested	1
6	Confounder	Adjusted for potential confounders	1
7	Limitations	Were discussed	1
8	Laboratory tests	Performance of anti-HCV test or PCR test Performance of confirmatory test	1 1

8–9 scores=high; 5–7 scores=moderate; ≤ 4 scores=low.
HCV, viral hepatitis C.

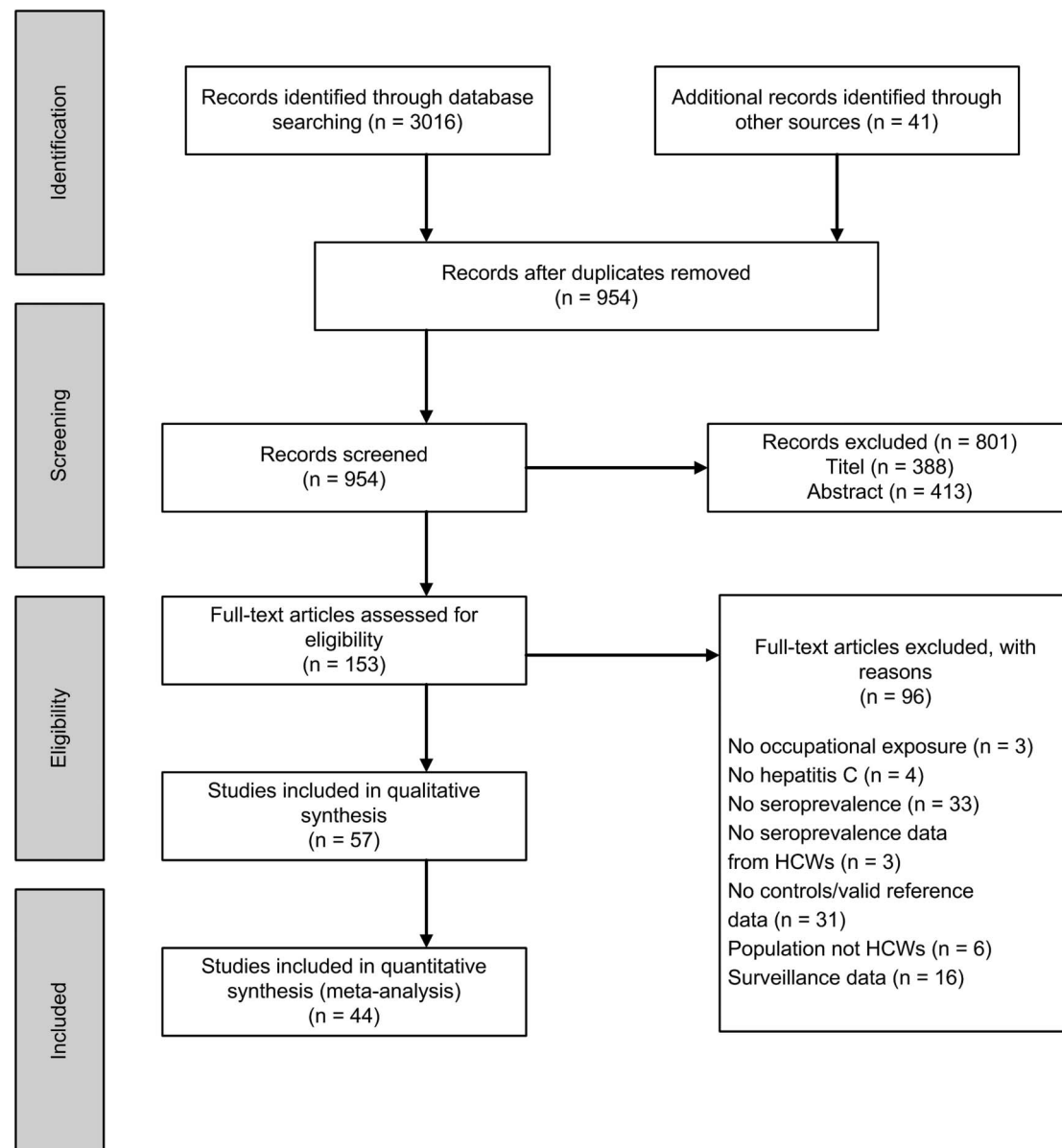


Figure 1 Selection process. HCWs, health care workers.

based and a hospital control group. Four studies used a population control and several other control groups, including risk groups such as dialysis patients and men who have sex with men.

Study design and quality

Fifty-one studies had a retrospective design and six a prospective design.^{24–29} The annual incidence was reported in two studies only. According to Puro *et al*,²⁴ the rate was 0.1%; and 0.15% according to Cooper *et al*.²⁶

The methodological quality was rated as high in seven studies, as moderate in 33 studies and as poor in 17 studies.

HCV detection

A HCV confirmation test was performed in 37 studies. Five studies used the same test for the confirmation as for the first test. There were differences between the studies with respect to the quality of the tests used (table 2).

HCV exposure among HCWs—a qualitative summary of studies not included in the meta-analysis

Thirteen studies could not be included in the meta-analysis because of missing case numbers (table 2). Increased HCV seroprevalence in HCWs in comparison to population controls was found in four out of seven studies of moderate methodological quality and in three out of six studies of low methodological quality. Cooper *et al*,²⁶ Goetz *et al*,⁵³ and Zaaijer *et al*⁶⁶ studied employees stratified by their exposure risk. All seropositive employees worked in areas with high exposure to blood contact (eg, dialysis, blood bank, laboratory), or reported prior NSI.²⁶ With the exception of Mijakoski *et al*,⁷³ all controls were from reference sources.

Meta-analysis

The main results are shown as plots in figure 2. Further results of pooling analyses and subgroup analyses are summarised in online supplementary table S3.

Table 2 Characteristics of studies included

Author/year	Country	Period	HCV tests	HCWs	n (n+)	Prevalence %	Controls	n (n+)	Prevalence %	Study quality (scores)*
Prospective studies										
Puro 1995 ²⁴	Italy	1992–1993	Anti-HCV 2, enzyme immunoassay RIBA 2	S	3073 (67)	2.2	Pr	11 000 (19)	1.7	High (8) ^{1–4 6–8}
Maillard 1996 ²⁵	France	1992–1993	ELISA 2, PCR	S	236 (7)	2.9	H	305 (2)	0.7	Moderate (6) ^{1 2 5 7 8}
Cooper ¹⁹⁹² ²⁶	USA	NA	EIA RIBA 2	S‡	243 (4)	1.6	Pr	–	0.4–1.4	Moderate (6) ^{1 2 4 7 8}
Ahmetagic 2006 ²⁷	Bosnia and Herzegovina	2003–2005	ELISA 3, HCV-RNA	S	1699 (6)	0.4	P	2000 (4)	0.2	Low (4) ^{1 2 5 8}
Daw 2002 ²⁸	Libya	1999–2001	ELISA	S	459 (9)	2	P§	1200 (14)	1.2	Low (4) ^{1 2 5 8}
Mihalyt 2001 ²⁹	Hungary	1986–1998	EIA 2, EIA 3, RIBA 3, PCR	M, NS, CS‡	477 (13)	2.7	Pr	–	0.73–1	Low (4) ^{1 2 8}
Retrospective studies										
Gershon 2007 ³⁰	USA	1999–2000	HCV 2, RIBA 3	S	216 (4)	1.9	H	94 (3)	3.2	High (9) ^{1–8}
Ozsoy 2003 ³¹	Turkey	1998–2000	Anti-HCV 3 IL, INNOTEST 3, RT-PCR, ELISA	S	702 (2)	0.3	P	5670 (23)	0.4	High (9) ^{1–8}
Klein 1991 ³²	USA	1985–1987	ELISA 1, RIBA	D	456 (8)	1.8	P	723 (1)	0.1	High (9) ^{1–8}
Sermoneta-Gertel 2001 ³³	Israel	1995–1997	EIA 3, RIBA 3	S	3657 (34)	0.9	H	630 (3)	0.5	High (8) ^{1–4 6–8}
Thomas 1996 ³⁴	USA	1991	ELISA 1 or ELISA 2, RIBA	NS	943 (7)	0.7	P	104,239 (417)	0.4	High (8) ^{1–5 7 8}
Struve 1994 ³⁵	Sweden	NA	EIA 2, Supplementary test	M, NS, L¶	797 (5)	0.6	H	83 (1)	1.2	High (8) ^{1–5 7 8}
Brackowska 2006 ³⁶	Poland	2003–2004	ELISA 3, Western blot LIA HCV Ab3	MS	558 (8)	1.4	P	510 (2)	0.4	Moderate (7) ^{1–3 5 6 8}
Fisker 2004 ³⁷	Denmark	1998	HCV 3, RIBA, PCR	S	960 (2)	0.2	H	479 (0)	–	Moderate (7) ^{1–5 8}
Ciorlia 2007 ³⁸	Brazil	1994–1999	ELISA 2	S	1433 (25)	1.7	H, P	872 (4) 2583 (6)	1.3 0.2	Moderate (7) ^{1–6 8}
Moens 2000 ³⁹	Belgium	1996–1997	EIA 3, Matrix Abbott und LIA, PCR	S‡	4480 (21)	0.4	H	426 (0)	–	Moderate (7) ^{1–3 6–8}
Thorburn 2001 ⁴⁰	Scotland	1994–1996	ELISA 3, PCR, RIBA-3	S, D	10,654 (27)	0.3	H	471 (3)	0.6	Moderate (7) ^{1–3 5 7 8}
Djeriri 1996 ⁴¹	France	1993–1994	EIA 2 RIBA2	S	283 (2)	0.7	H	93 (0)	–	Moderate (7) ^{1–3 5 6 8}
Villate 1993 ⁴²	Spain	1991–1992	ELISA 2, PCR, RIBA 2	M, L, NS¶	874 (14)	1.6	P	547 (2)	0.4	Moderate (7) ^{1–5 8}
Montella 2005 ⁴³	Italy	1991	ELISA 1, ELISA new generation	M, NS, L¶	578 (32)	5.5	H	91 (6)	6.6	Moderate (7) ^{1 2 4–6 8}
Kaabia 2009 ⁴⁴	Tunisia	2005	ELISA Murex 4, ELISA AxSYM Abbott	M, L, P, Mw¶	737 (9)	1.2	H	104 (0)	–	Moderate (6) ^{1–3 5 8}
Irani-Hakime 2001 ⁴⁵	Lebanon	1999	SM-HCV rapid test, MEIA HCV 3, PCR	S	502 (2)	0.4	P	600 (1)	0.2	Moderate (6) ^{1–3 5 8}
Campello 1992 ⁴⁶	Italy	1989–1990	ELISA, HCV neutralisation test	S	407 (5)	1.2	P	253 (2)	0.8	Moderate (6) ^{1 2 4 5 8}
Polish 1993 ⁴⁷	USA	1983	Anti-HCV 1 Abbott, HCV neutralisation assay Abbott	S	1350 (22)	1.6	H	257 (1)	0.4	Moderate (6) ^{1 2 5 6 8}
Perez Trallero 1992 ⁴⁸	Spain	NA	ELISA 2, RIBA 2	S	251 (4)	1.6	P	377 (8)	2.1	Moderate (6) ^{1 2 4 5 8}
Takahama 2005 ⁴⁹	Brazil	NA	ELISA 3, PCR, AxSym Abbott 3	D	267 (1)	0.4	P	88,241 (304)	0.3	Moderate (6) ^{1 2 4 7 8}
Trevisan 1999 ⁵⁰	Italy	NA	EIA, RIBA 3	S	809 (9)	1.1	H	408 (8)	2	Moderate (6) ^{1 2 4 5 8}
Weber ²⁰⁰¹ ⁵¹	Switzerland	1999	EIA, EIA3, PCR, Immunoblot	D, DS	1056 (1)	0.1	Pr	–	0.5–1	Moderate (6) ^{1 2 4 7 8}
Shapiro ¹⁹⁹⁶ ⁵²	USA	1991	Immunoassay 1, supplementary neutralisation assay	M	3262 (27)	0.8	Pr	–	0.09–0.36	Moderate (6) ^{1 2 4 7 8}
Goetz ¹⁹⁹⁵ ⁵³	USA	NA	EIA 2, RIBA 2, Ortho, PCR	M, D, NS, L‡	241 (5)	1.3	Pr	–	0.3	Moderate (6) ^{1 2 4 7 8}
Ahmed 2012 ⁵⁴	Pakistan	2007–2009	ETI-AB-HCV-4	S	41 (7)	17.1	P	1959 (103)	5.3	Moderate (5) ^{1 4–8}
Fischer 2000 ⁵⁵	USA	1998	PCR	S	502 (0)	–	H	926 (2)	0.2	Moderate (5) ^{1 2 5 7 8}
De Mercato 1996 ⁵⁶	Italy	1995	RIBA 2	S	472 (12)	2.5	P	285 (8)	2.8	Moderate (5) ^{1 2 4 5 8}

Continued

Table 2 Continued

Author/year	Country	Period	HCV tests	HCWs	n (n+)	Prevalence %	Controls	n (n+)	Prevalence %	Study quality (scores)*
Olubuyide 1997 ⁵⁷	Nigeria	1995	HCV 3-enzyme Immunoassay Murex	M, D	75 (8)	10.7	P	25 (3)	12	Moderate (5) ^{1 2 4 7 8}
Al-Sohaibani 1995 ⁵⁸	Saudi Arabia	1992–1994	UBI HCV EIA, RIBA or LiaTEK HCV 3	M, MS†‡	330 (8)	2.4	P	292 (5)	1.7	Moderate (5) ^{1 2 5 8}
Soni 1993 ⁵⁹	South Africa	1991	EIA 2, EIA 2, Abbott neutralisation EIA	NS	212 (0)	–	P§	35 685 (92)	0.3	Moderate (5) ^{1 2 5 8}
Oguchi 1992 ⁶⁰	Japan	1989	ELISA 1 or 2,	S	150 (3)	2	P	704 (7)	1	Moderate (5) ^{1 2 4 5 8}
Nakashima 1993 ⁶¹	Japan	1987–1988	ELISA, RIBA	S	1097 (11)	1	P	526 (5)	1	Moderate (5) ^{1 2 5 8}
Fujiyama 1992 ⁶²	Japan	NA	ELISA anti-C100	S	152 (1)	0.7	P	919 (14)	1.5	Moderate (5) ^{1 2 5 8}
Germanaud** 1994 ⁶³	France	NA	ELISA 2, RIBA 2	S	430 (4)	0.9	H	180 (3)	1.7	Moderate (5) ^{1 2 5 8}
Jindal† 2006 ⁶⁴	India	2003	Hep-Chex C	S	100 (4)	4	Pr	–	1.6	Moderate (5) ^{1 2–4 8}
Kuo† 1993 ⁶⁵	Taiwan	1990–1991	EIA 1, EIA 2, PCR	D	461 (3)	0.7	Pr	–	1	Moderate (5) ^{1 2 4 8}
Zaaijert 2012 ⁶⁶	The Netherlands	2000–2009	AxSYM HCV, RIBA 3, PCR	S‡	729 (1)	0.1	Pr	–	0.6	Moderate (5) ^{1 2 7 8}
Zuckermant 1994 ⁶⁷	Scotland	1986, 1991	EIA 2, RIBA 2	S	1053 (3)	0.3	Pr	–	0.3	Low (4) ^{1 2 8}
Jochen** 1992 ⁶⁸	Germany	1992	EIA 2, Immunoblot 2	S	1033 (6)	0.6	P	2113 (5)	0.2	Low (4) ^{2 5 8}
El Gohary 1995 ⁶⁹	Egypt	1990–1992	EIA 2	S	78 (6)	7.7	P §	271 (39)	14.4	Low (4) ^{1 2 5 8}
Polywka 1991 ⁷⁰	Germany	NA	ELISA	S	217 (6)	2.8	P	500 (2)	0.4	Low (4) ^{1 2 5 8}
Hindy 1995 ⁷¹	Egypt	NA	ELISA, Abbott, ALT	DS	70 (1)	1.4	H	35 (6)	17.1	Low (4) ^{1 4 8}
Khan 2011 ⁷²	Pakistan	NA	Immunochromatography test, PCR	S	794 (34)	4.3	H	30 (0)	–	Low (4) ^{1 2 4 8}
Mijakoski† 2012 ⁷³	Macedonia	NA	anti-HCV Ab	NS	54 (0)	–	H	32 (0)	–	Low (4) ^{1 4 5 8}
Kondili 2007 ⁷⁴	Albania	NA	EIA 3	S	460 (3)	0.7	H	22 (0)	–	Low (3) ^{1 5 8}
Libanore** 1992 ⁷⁵	Italy	NA	Immunoassay	S	1008 (41)	4.1	Pr	3572 (34)	1	Low (4) ^{1 2 5 8}
Mujeeb† 1998 ⁷⁶	Pakistan	NA	EIA	S	114 (5)	4.4	Pr	–	0.7	Low (4) ^{1 2 4 8}
Sarkari† 2012 ⁷⁷	Iran	2009–2010	ELISA 3	S	212 (9)	4.2	Pr	–	0.1–0.9	Low (4) ^{1 2 7 8}
Vardas 2002 ⁷⁸	South Africa	1996	ELISA 3, PCR	S	362 (7)	1.9	H	37 (0)	–	Low (3) ^{1 2 8}
Shoaeit 2012 ⁷⁹	Iran	2010	ELISA	L	203 (0)	–	Pr	–	0.2	Low (3) ^{1 2 8}
De Luca** 1992 ⁸⁰	Italy	1990	NA	S	945 (45)	4.8	P§	3575 (39)	1.1	Low (2) ^{2 5}

() In bold letters: cases confirmed by second test.

*Fulfilled item for quality assessment—see table 1.

†Not included in meta-analysis.

‡Stratified by working area/exposure.

§Further control groups NA.

¶Stratified by professional groups.

**Editor letter.

CS, cleaning staff; D, medical dental staff; DS, dental staff (Medical and Non-Medical); EIA, enzyme immunoassay; H, hospital controls; HCV, viral hepatitis C; HCWs, healthcare workers; L, laboratory staff; M, medical staff; MS, medical students; Mw, midwives; NA, not available; NS, nursing staff; P, population-based controls; Pr, reference data on population-based controls; RIBA, the recombinant immunoblot assay; S, staff/ HCWs.

A total of 44 studies were included in the pooled analysis (seven high quality studies, 26 moderate quality studies and 11 low quality studies—table 2). The pooled analysis of all studies showed a significantly increased OR of 1.5 (95% CI 1.15 to 2.06) for a HCV infection among HCWs compared to controls, with significant evidence of heterogeneity ($\chi^2=110.8$, $p<0.001$,

$I^2=61$, see online supplementary table S3). The increased prevalence of HCV infection in HCWs was also observed in the 14 studies with high and moderate methodological quality, using population control groups and confirmatory tests (OR 1.6; 95% CI 1.03 to 2.42, no evidence of heterogeneity, figure 2).

After stratification by publication period, HCWs were found to have a statistically significant increased prevalence of HCV infection in the period 1989–2000 compared with all controls (OR 1.3; 95% CI 1.09 to 1.63). For the period 2000–2014, the pooled effect estimate was the same, but without a statistically significant increase (OR 1.3; 95% CI 0.89 to 2.02). As there are only a few current studies, it was not possible to conduct a test for time trend by subgroups (see online supplementary table S3).

The following analyses were based on high and moderate quality studies only.

Study region

Pooled analysis of studies from countries with comparably low HCV prevalence in Europe (Belgium, Denmark, France, Scotland, Sweden) and the USA showed a significantly increased prevalence of HCV infection in HCWs compared with controls (OR 2.1; 95% CI 1.31 to 3.42, figure 2). Further stratification by population-based controls could not be performed because of considerable variability between the studies ($I^2=70$). Pooled analysis of Japanese studies showed no increased HCV prevalence in HCWs (OR 1.1). Stratification of studies from the other countries by individual regions resulted in a statistically significant increased HCV prevalence in HCWs only for North Africa, the Middle East and South Asia (OR 1.9; 95% CI 1.10 to 3.15), compared to controls (see online supplementary table S3).

Gender

Six studies reported anti-HCV prevalence stratified by gender. By pooling studies using population-based controls with confirmatory tests, a significantly increased prevalence was observed only for male HCWs (women OR 1.5; 95% CI 0.45 to 5.24; men OR 3.1; 95% CI 1.21 to 7.99).

Professions

Medical staff: For medical personnel, pooled analysis of studies with confirmatory tests gave an OR of 2.7 (95% CI 1.65 to 4.51, figure 2). For medical staff excluding dentists, the OR was 2.2 (95% CI 1.30 to 3.77) for a HCV infection compared to population-based controls (see online supplementary material table S3).

Dental staff (medical and non-medical): Pooled analysis of studies with confirmatory tests gave an OR of 3.5 (95% CI 1.37 to 9.15, figure 2) for a HCV infection among dental staff compared to controls. Further stratification could not be performed because of considerable variability between the three studies.

Nursing staff: The pooled analysis of studies with confirmatory tests showed an OR of 1.7 (95% CI 0.86 to 3.31) for nursing staff compared to the population-based controls (see online supplementary table S3).

Laboratory staff: Pooled analysis of studies with confirmatory tests gave an increased OR of 2.2 (95% CI 1.10 to 4.39, figure 2) for a HCV infection in laboratory staff compared with all controls.

Professionals at high risk for blood contacts: Six sources contributed data on the following professions/working areas performing EPPs: surgeons, midwives, microbiologists, pathologists, blood bank and dialysis staff. All studies were published before 2000. The pooled analysis shows a statistically significant increased OR of 2.3 (95% CI 1.51 to 3.54) for a HCV infection

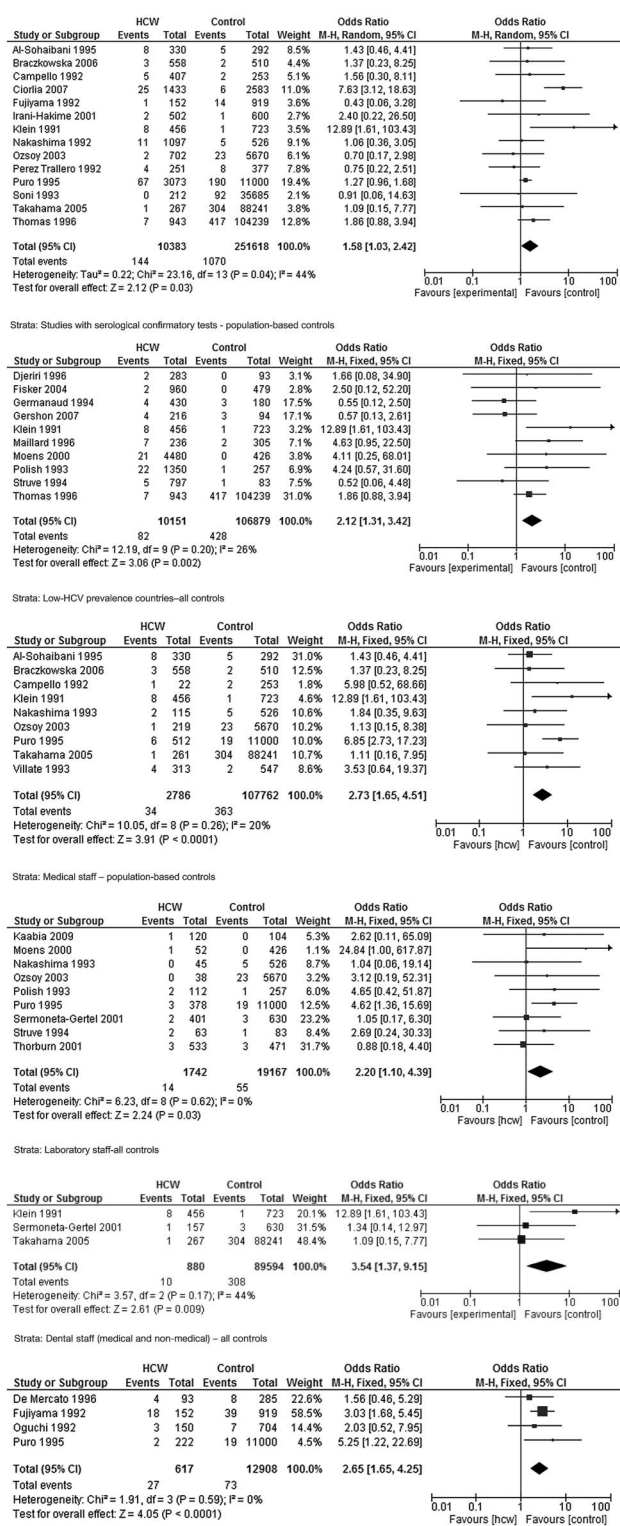


Figure 2 Forest plots of high and moderate quality studies on hepatitis C among healthcare workers. HCWs, health care workers.

among HCWs compared with all controls and of 2.7 (95% CI 1.84 to 5.53, [figure 2](#)) compared to population-based controls.

Heterogeneity and sensitivity analysis

Heterogeneity was present when pooling all studies. Pooling the studies with high and moderate methodological quality only, reduced heterogeneity. Further stratification was performed related to performance of confirmatory tests. In addition, individual studies were then sequentially excluded from the analysis in order to verify their influence on the pooled estimate.

Publication bias

The funnel plot did not show evidence of publication bias (see online supplementary figure S3), nor did Egger's linear regression show significant evidence of funnel plot asymmetry (intercept 0.19, 90% CI 0.33 to 0.71, $p=0.47$).

DISCUSSION

This is the first systematic review to perform a meta-analysis on the prevalence of HCV infection among HCWs in comparison to controls. The pooled analysis of high and moderate quality studies gave a statistically significant increase in OR of 1.6 for HCV infection among HCWs compared to population-based controls. Stratified pooled analysis of studies with confirmatory tests from countries with comparable low HCV prevalence also resulted in a statistically significant increase in OR for HCWs in comparison to controls (OR 2.1). Stratification by occupational groups demonstrated an increased prevalence among *medical staff* (OR 2.2), *laboratory staff* (OR 2.2) and *dental staff* (medical and non-medical, OR 3.5), compared to controls. However, due to the few studies found for dental staff, further stratification by profession could not be performed. In addition, the pooled effect estimated is mainly caused by one high quality study with a wide CI.³² When the pooled analysis was stratified by *nursing staff*, no significant increase in OR was found. A differentiated examination of activity profile-related occupational hazards was carried out for this profession in only a few studies. This lack of differentiation may lead to underestimation of the occupational risk of infection due to exposure misclassification. This happens particularly when HCWs who are frequently exposed to blood while performing EPPs are examined in combination with less exposed HCWs in the same job category. Pooled analysis for each individual group—such as cleaning staff—was not possible as the studies were few and their methods heterogeneous in design, HCWs examined, serological testing and controls. This diversity is the main reason for the lack of consensus in the assessment of the occupational risk of HCV infection in HCWs.^{81–83} Additionally, it is difficult to quantify the occupational risk given to a specific profession, such as for laboratory staff, as there is no systematic record of how exposure depends on the activity.⁸⁴ To estimate HCV prevalence in HCWs due to specific work profiles, we conducted an exemplary pooled analysis of professions that performed EPPs in accordance with the criteria of Trevisan *et al.*⁵⁰ The pooled analysis shows a significantly increased OR of 2.7 for these employees in comparison to the population-based controls. However, the results of this subgroup analysis are based only on studies published before 2000. The assessment of personal risk factors for a HCV infection was not performed consistently in the investigated studies, particularly in studies published earlier. Those examinations were conducted prior to the Needlestick Safety and Prevention Act (NSPA). Both in the USA and in Europe, guidelines have been issued since 2000 that aim to prevent exposure to blood, for example, from NSI.^{6 85}

The results of studies that could not be included in the quantitative analysis did not conflict with the results of the meta-analysis. Professions that performed EPPs are exposed to NSI, with a HCV transmission rate of 1.8% after an NSI according to Henderson,⁸³ Riddell and Sherrard,⁸⁶ and Baldo *et al.*⁸⁷ The results of an American multicentre study performed in 2006 showed that occupational exposure was greater in male HCWs.⁸⁸ The authors observed that men were three times more frequently infected than their female colleagues. In this context, bivariate analysis showed that glove use when performing invasive work was significantly associated with the female gender. According to the reviews of Kubitschke *et al.*⁸ and Goniewicz *et al.*,⁸⁹ NSIs were more frequent in inexperienced personnel. Current findings on the incidence of NSI in the health service show that nursing^{6 88 90} and medical personnel⁸⁸ are the most frequently affected professional group. According to Butsashvili *et al.*⁸⁸ the highest number of exposures to NSI is in dialysis work. The most recent research on dialysis staff (2006–2010) concluded that there had been no decrease in the number of observed NSIs suffered by staff.⁶

Strengths and limitations

This is the first meta-analysis to examine the prevalence of HCV infection in HCWs compared to controls. However, the mostly retrospective studies included some recent studies. In addition, older studies tend to report higher anti-HCV prevalence rates than more recent studies (as confirmed by Larney *et al.*⁹¹). As there are only a few current studies, it was not possible to draw reliable conclusions about a time trend. Most of the population-based controls were blood donors. Individuals at risk of HCV infection in the general population were probably not included. The results of the studies that referred to reference populations must also be viewed critically. HCWs and controls may not have been tested under identical conditions. Few studies have examined how occupational hazards depend on the activity profile. This lack of differentiation may lead to underestimation of the occupational risk of infection for specific HCWs. So, the present results reveal a strong demand for further differentiated research.

Quality of serological testing

The quality of the confirmatory tests used clearly differs between individual studies. This is due to the development of better detection methods over time, the quality of the procedure or the fact that there is no fundamental difference between the antigens used in the screening and the confirmatory tests. Owing to the limitations in the sensitivity of the first anti-HCV tests (false negatives), earlier studies tended to underestimate seroprevalence. In contrast, limitations in specificity lead to false positive results. This may result in non-differential misclassification, which again is most likely to lead to decreased effect estimates.

Assessment of personal risk factors

The personal risk factors for HCV infection were not recorded consistently in the studies. The risk factors, such as use of injected drugs and injury-prone sex (men with men) were not collected in many studies, especially the earlier ones. The 1998 report of the US Center for Disease Control and Prevention (CDC) on the known risks of HCV infection identified drug use and injury-prone sex as the most common causes.¹⁵ Of the six studies that allow stratification by gender, only two examined these confounding factors, which are associated with a higher

risk of non-occupationally acquired HCV infection, especially among men.^{32 36}

CONCLUSION

This meta-analysis shows a statistically significant increase in the prevalence of HCV infection in HCWs compared to controls. Medical and laboratory personnel, and staff members who perform EPPs, are particularly affected. For other professions, no adequate calculation of a pooled estimate was possible. Prevalence of HCV infection has probably decreased since 2000, due to improved prevention. However, this needs to be investigated further. To analyse HCWs' occupational risk of infection, prospective studies are needed that focus on HCWs in terms of specific work profiles bearing in mind the importance of assessment of personal risk factors for infection. Contact with blood, for example, from NSI, is associated with a risk of infection and continues to be the major threat to the health of HCWs. Targeted prevention measures must be based on the epidemiological detection and evaluation of work-related accidents. Readily accessible reporting and treatment procedures, and the use of safe practices for working with blood, can help to minimise occupational exposure.

Collaborators Melanie Harling.

Contributors CW conceived the study protocol, performed the study selection, data extraction, quality assessment and statistical analysis, and wrote the first draft of the manuscript. CP was involved in performing data extraction, quality assessment and statistical analysis and made substantial contributions toward revising the first draft. BL performed the study selection and assessment, and made substantial contributions towards revising the first draft. ML made substantial contributions toward revising the first draft. AN coordinated the study, amended the study protocol, assisted in study selection and statistical analysis, and made substantial contributions toward revising the first draft.

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The prevalence of hepatitis C among healthcare workers: a systematic review and meta-analysis

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