

Table 3. Study populations and results of the seroprevalence studies.

Reference	Study	Study population §	Exposure	Prevalence and	DRR, MA **
Country	design ‡		surrogate ¶	risk estimate	Comments
Time period †			Outcome		
<u>Study populations and results of the eligible studies. *</u>					
Lerman et al. (1999) ²⁸ Israel 1993-1994	HP	1130 patients with clinical HA in a labour force of about 3,700,000 Standardised incidence ratios calculated using 2 standard populations R: 681 lost cases of similar gender and age. No specific information on vaccination available.	Belonging to occupational group “cleaning and sewage workers” (n=59,480) clinical HA identified in 1993- 1994.	SIR: 0.88 and 0.95 (99%CI: 0.38-2.03 and 0.38-2.42, with standard population 1 and 2, respectively)	DRR: NA. Exclusion criteria were age less than 18 y, contact with a family member suffering from HA; travelling to hyperendemic area before the occurrence of the disease, being a tourist, prisoner, and soldier on active duty. MA: age, gender, ethnicity, and time of immigration to Israel controlled for. Israel is a country endemic for HA.

Table 3. continued

Brugha et al. (1998) ²⁹ United- Kingdom (London area) 1995-96	CS 4	E: 147 high risk employees from the 3 main drainage depots and 3 large sewage treatment works C: 81. Age (all participants): 39 (NI) Probably males. P: 85 and 68 % in E and C, respectively. Exclusions and V: see comments.	Exposure to raw sewage (according to manager) ED, EI, EF (frequency of splashes; structured questionnaire) IgG clinical diagnosis of viral hepatitis	E: 46 % (sewerage workers) C: 30 % ORs: raw sewage some of the time: 1.14 (0.50-2.59) raw sewage most of the time: 3.73 (1.48-9.37)	DRR: increase (n.s.) in seropositivity with exposure risk as defined by manager (46, 40, 29, 30 % in sewerage workers, flushers and fitters, electricians and supervisors, and unexposed workers, respectively). Increasing OR with frequency of exposure: see OR. MA with numerous confounding factors (travelling in endemic areas, age, socio-economic level, etc.) Lost cases unlikely to have caused a major bias. 13 participants secondarily excluded (10 vaccinated subjects and 3 with ambiguous test results). Exposure to raw sewage most of the time may represent a subgroup with particularly high exposure.
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Cadilhac and Roudot-Thoraval (1996) ³⁰	CS 3	E: 155 sewage workers Age: 85.2 % older than 29 y. 125 M (80.6 %).	CO ED (about 10 ± 8)	E: 60 % C: 47.1%	DRR: no DRR found in multivariate analysis. The seroprevalence of anti-HAV antibodies was very similar in the 3 subgroups defined by EF.
France (Val de Marne) 1993		C: 70 employees from the same firm. Age: 90 % older than 29 years. 19 M (27 %).	EF (3 grades) “total specific antibodies”	OR: 2.15 (1.15-4.00)	Detailed MA: age, gender, educational level, number of siblings, travelling in endemic areas as well as occupational exposure (qualitative indicator, EF, and ED).
		P (E +C together): 82 %.			Two other papers refer to the same population
		R: NI Exclusion of immunized subjects: NI			(Cadilhac and Roudot-Thoraval ^{50 51}).
					The publication by Schlosser and Roudot-Thoraval (see below) might include part of the same population.

Table 3. continued

Benbrik et al. (2000) ³¹ France (City of Paris) 1995-1996	CS 2	E: 201 sewage workers and 390 water-purification station workers. Age: 41 and 39 (23-59 and 20-60) respectively. M only C: 643 administrative workers. Age: 42.5 (21-63) M only. Education level, country of birth, V: see comment. Overall P: 85.5 %. R: NI	CO ED Occupational risk factors ("soiled earth", "floating corpses", etc.) total antibodies (IgG and IgM)	E: 71 % C: 67 % OR(*): 1.17 (0.91-1.50)	DRR: not explored in a MA. MA: factor analysis identified 5 subgroups (non-exposed workers and 4 subgroups of exposed workers). No clear subgroup-specific patterns of occupational risk factors appeared. Results very descriptive (no a priori hypothesis tested in a logistic regression model). No clear definition of the types of non-occupational and occupational risk factors (for example "floating corpses"). Education level and country of birth differed between both groups. Vaccination status recorded but not included in multivariate analysis.
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Levin et al. (2000) ³²	CS 2	E: 100 sewage workers Age 42.7 (22-67) M only R: NI C: 100 controls matched for age, sex, education, and smoking V: NI	CO EF: daily exposure in 63 % of the cases ED (0.5-35) IgG	E: 82 % C: 91 % OR: exposure to sewage removed from the logistic regression except seniority (see DRR)	DRR: no association with frequency of exposure or use of protective equipment. Increased seniority predicted less seropositivity with an adjusted OR of 0.8 (0.7-0.9). MA: age, education, smoking, seniority, exposure frequency, and several indicators of protective equipment considered in the analysis Israel is a country endemic for HA
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Trout et al. (2000) ³³ U.S.A. (Ohio) 1998-1999	CS 2	E: 163 workers (waste- water treatment plant and wastewater maintenance) Age: 46-47 (23-74) F: 2-3 %. A 2 nd plant could not be surveyed. C: 139 workers (recreation centres, electrical workers) Age: 38-39 (20-63). F: 40 and 4%, respectively P: 74-88 % R: NI All workers unimmunized	CO EI (no further information) Saliva IgG Prevalence of jaundice or hepatitis	E: 18 and 31 % in treatment plant and maintenance workers, respectively. C: 20 and 4 % in recreation centres and electrical workers, respectively. Adjusted prevalence ratios (95%CI): 1.3 (0.7-2.4)	DRR: no significant DRR. MA: models including occupational factors (exposure, protective equipment, hygiene) as well as age, gender, travelling in endemic areas, education, income, race, household contact, foreign birth. Large differences (up to 20 times) between some sub- groups regarding gender, race, income, and education were found. Thus, crude prevalence rates are hardly comparable. Adjusted prevalence ratios calculated with multivariable regression models. The authors could not account for the low prevalence in electrical workers (however this subgroup was younger and had a higher income).
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Weldon et al. (2000) ³⁴ U.S.A (Texas) 1996-1997	CS 2	E: 359 wastewater workers. Age: 41.2 (NI) M: 88.4 %. Hispanic: 18.9 %. C: 89 drinking water workers. Age: 41.3 (NI). M: 89.3 %. Hispanic: 27 %. P: "approximately 65 - 85 %". R: convenience sample. V: see comment	CO EI ED EF IgG and IgM	E: 28.4 % E, Hispanics: 57.4 % E, non-Hispanics: 21.6 % C: 23.6 % C, Hispanics: 50 % C, non-Hispanics: 13.8 % OR: 1.6 (0.6-4.5) in Hispanics and 2.4 (1.0-5.7) in non- Hispanics	DRR: OR for employment in the wastewater industry for more than 7 y and for skin contact with sewage at least once a day of 1.9 (1.1-3.6) and 1.8 (1-3.3), respectively. MA: travelling to endemic areas not mentioned. In the model used for assessment of DRR ethnicity was no longer considered. V: anti-HAV negative participants with a history of HA vaccination not excluded from analysis (anti- HAV assay not always capable of detecting the low levels of anti-HAV that may accompany vaccine-induced immunity).
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DeSerres	CS	E: 76 sewer workers			
et al. (1995) ³⁵	2	P: 75% of all	ED at this	E: 54 %	DRR: no association of seropositivity with ED;
Canada (Quebec		municipal sewer workers	work (10;	C: 49 %	MA: socio-economic level and travelling
City area)		(Quebec City area)	1-30)		to endemic areas not considered
1993		Age: 41 (28-64) (74M/2F)	Ig type: NI	OR(*): 1.20	
		all born in Canada.		(0.67-2.17)	R of C group: C "assumed to represent a valid
		R: those who refused did	history of jaundice		sample of the overall population".
		not differ from participants	and hepatitis		V: no subject had been vaccinated according to
		by age and ED.			DeSerres ⁵² .
		C: 2 outpatients undergoing			
		lipid testing pro worker			
		(matched on age and sex).			
		P, R, V: see comments.			

Table 3. continued

Schlosser	CS	E: 110 workers exposed	CO	E: 60.9 %	DRR: not tested in an MA with confounding variables.
Roudot-Thoraval (1995) ³⁶	2	to sewage (made of 4 subgroups with different exposure types).	ED (10.3; 1-36)	C: 44.5 %	MA: travelling to endemic areas not considered. Gender was not a matching criterion. (21 % female workers).
France (region of Paris) Before 1995		C: 110 workers from the same firm matched on age ($\pm 5y$) and education. Age: 36.5 (20-58). M: 79 %. R, P: NI. Exclusion of immunized workers: NI	IgG or total antibodies history of jaundice	OR: 2.4 (1.6- 3.1)	Three other publications or abstracts refer to the same population (Schlosser and Roudot-Thoraval ^{53 54} , Roudot-Thoraval and Schlosser ⁵⁵). No new original data in a further letter (Schlosser and Roudot-Thoraval ⁵⁶).

Table 3. continued

Heng et al. (1994) ³⁷ Singapore 1992-1993	CS 2	E: 600 sewage workers P: 77 % of those deployed in Singapore. R: NI. Age: 20-≥50. M: 95 %. Chinese: 36.3 %, Indians: 29.5 % C: 453 subjects attending routine health checks. Age: 20-≥50. F: 66.2 % Chinese: 92.3 % Indians: 3.5 %. P, R: NI. All subjects unimmunized.	ED in current job total Ig (IgG and IgM)	E: 72.7 % C: 50.8 % OR: 2.2 (1.6-3.1)	no DRR in multivariate analysis MA: age, sex, ethnic group, past medical history and educational level considered. Shellfish consumption not included although it may have been an important confounding variable (Goh et al., ^{57 58}). Older age, lower socio-economic level, longer duration of employment, higher frequency of illness collected in the Indian sewage workers who were hardly represented in the control group
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Skinhoj et al. (1981) ³⁸	CS 2	E: 77sewer workers Age: Md 44 (21-65). M only	ED in this plant Md: 9 (1-36)	E: 80.5 % C1: 60.5 %	DRR: no association between prevalence rates of anti-HAV antibodies and ED or EF after adjusting for age. MA: unclear information; socio-economic status and travelling in endemic areas not considered.
Sweden (Copenhagen) Before 1981		C1: 81 gardeners C2: 79 clerks (matching: age, sex, duration of employment). All subjects were municipality workers P: 96 % (E, C1, C2). No information on the third control group (street workers). V: before 1992.	EF Probably total IgG jaundice or liver disease unrelated to gall bladder disease	C2: 48.1 % OR(*): 2.70 (1.24-5.91) compared with C1 4.46 (2.06-9.75) compared with C2	

Table 3. continued

Khuder et al. (1998) ³⁹	CS 1	E: 150 wastewater treatment workers age: 43.7 (SD: 9.1) 130 M. P: about 62 % (30-100 %). R: NI. C: 54. Age: 44.9 (SD: 8.2). 52 M. P: similar to E group. R: NI. V: see comment	high vs low exposure risk (2/3 vs. 1/3) ED: 14.1 (SD: 8) Jaundice/HA (self-administered questionnaire)	NA OR: NA	DRR and MA: inapplicable Unclear whether the immunity of control and exposed workers was comparable before employment. Nothing is known about socio-economic level, travelling to endemic areas, seropositivity, and vaccination No anti-HAV antibodies determined.
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Leverly et al. (1996) ⁴⁰ France (region of Touraine) 1993-1994	CS 1	E1: 47 workers ("heavily exposed", i.e. work in sewers, septic tanks, and /or with cleaning pumps). E2: 15 workers ("less exposed", i.e. sewage works). Age: 36 (20-57). M only. P: 77.5 %. R: NI. C: 62 subjects matched according to age, sex, and socio-economic status. V: NI.	ED (≤ 5 and > 5) EI ("heavily" and "less exposed", respectively). anti-HAV anti-bodies (type unknown)	E: 61.3 % C: 51.6 % OR(*): 1.48 (0.68-3.23)	DRR: "heavily" exposed workers with > 5 y exposure more often seropositive than their controls (92.3 vs 61.5 %, respectively). MA: further counfounders searched for but not used in an MA Relative risks were calculated whereas ORs would have been more appropriate and have given less or non-significant results. Power rather low for subgroups analyses according to age classes. The paper by Leverly et al. ⁵⁹ is an abstract referring to the same population
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Frolich and Zeller (1993) ⁴¹	CS 1	E: 408 sewage exposed employees (3 subgroups; age: 40.8, 41.1, 40.3; SD: 9.6, 9.9, 12.3). Probably M. P: NI C: 202 subjects from the same plant. Age: 40 (SD: 10.5). Probably M. P: NI. Workers from endemic regions excluded. All subjects unimmunized.	CO total Ig (IgG and IgM)	E: 37.7 % C: 30.2 % COR: see under comment	DRR: not explored (exposure defined qualitatively). No matching (gender, socio-economic level) and no MA Non-significant ORs in all 3 subgroups: 1.41 (0.96-2.09), 1.20 (0.56-2.51), 1.58 (0.69-3.62), for workers on the sewage treatment area (n=332), workers on the pumping station, and workers maintaining the flow of a section of a river, respectively. Confidence intervals calculated on the basis of the data presented by the authors.
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Poole and Shakespeare (1993) ⁴²	CS 1	E: 40 sewage workers Age: 42.2 (21-58). Probably M. P: 100 %.	CO IgG	E: 57.5 % C: 33.3 %	DRR: not explored. MA: no MA with age, travelling to endemic areas, and social class.
United Kingdom (West Midlands) Before 1993		C: 18 road workers. Age: 38.7 (20-62). Probably M. P: NI. "No subject vaccinated in the previous 6 months"		COR: 2.71 (0.74-10.23)	The authors reported a COR of 2.6 (1.04-6.51) by comparison with another control group. However, road workers were specifically selected to take into account age and social class of the potentially exposed workers (Maguire ⁶⁰) and the selection of the second control group may have been biased (Poole and Calvert ⁶¹).
					Another paper refers to the same population (Shakespeare and Poole ⁶²).

Table 3. continued

Chriske et al. (1990) ⁴³	CS 1	E1: 93 sewer workers. P: 67.8 %. R: NI.	CO	E1: 65.6 % E2: 56.0 %	DRR: not explored. MA: no MA.
Germany (Cologne) Before 1990		E2: 84 workers from sewage treatment works. P: 93.3 %. E1 and E2: age: NI (21-65), gender: NI, German workers only. C: 1831 persons recruited from the general population. Age: NI (21-65). Gender, P, and R: NI. V: before 1992	anti-HAV anti- bodies (type: NI).	C: 31.2 % OR(*): E1: 4.20 (2.65-6.66) E2: 2.80 (1.76-4.45)	Gender was not a matching criterion. The data presented by Hofmann et al. ⁶³ are taken from this study and not from an independent study population.

Table 3. continued

Ross et al. (1998) ⁴⁴	RS	1037 cases of occupationally acquired infectious diseases	occupation and industry (standard classification)	no case in sewerage workers	DRR and MA: NA
United Kingdom October 1996- September 1997		Age and gender both specified for only 600 cases R: probably non- representative study population V: NA.	diagnosis of HA made by consultants		No overlap with the study reported by the PHLS working group (1991) (see above) Comparison with other surveillance schemes suggests differential underreporting of eligible cases and added an estimated total of 257 cases.

Table 3. continuedStudy populations and results of the non-eligible studies.

Clark et al. (1984) ⁴⁵ U.S.A. (Memphis, Cincinnati, Chicago). 1975-1978	Cohort (and CS ana- lyses)	E: 339 workers (sewer maintenance, sewage and activated sludge treatment). C: 185 subjects (highway maintenance, water treatment plant, gas and electric public utility). Exact gender and age distribution: NI. P, R: NI. V: before 1992.	CO ED (with 2 subgroups less than 75 months and 75 and more). Air and waste- water monitoring. anti-HAV anti- bodies (type NI) every quarter and illness data	Seroconversion in 1/180 exposed and 1/69 non- exposed worker who were initially seronegative (exact duration of follow- up for these subjects: NI).	DRR and MA (tested in cross-sectional analyses): exposure effect (defined qualitatively or by ED) n.s. in MA including age, race, and socio-economic index (0.15 ≤ p ≤ 0.6).
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PHLS working group (1991) ¹⁵	CC	3000 cases and controls V: NA	Indicator of exposure: NI	No increased risk in sewage workers was found according to Maguire ⁶⁰ .	No further information available. A later full account of the study results was announced in this paper. However, the corresponding publication could not be located.
England and Wales (1990-1991)			Interview Salivary IgG and IgM		

Table 3. continued

Salano and Copello (1998) Genoa ⁴⁶ Before 1998	CS	E: 126 (maintenance of sewage network; waste water treatment plant (3 exposure subgroups). M: NI. C: general population. V: NI.	3 exposure subgroups hepatitis A markers	Decreased risk in exposed workers especially in those aged less than 30 years (see comment) OR: NI	Seroprevalence > 80 % in all three age classes in control group (< 31, 31-40, > 40 y). In exposed group seroprevalence was about < 5, 25, and 78 % in the same age classes.
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Arvanitidou et al. (1998) ⁴⁷ Greece (Thessaloniki) before 1998	CS	E: 167 (M and F) P: 82.2 %. C: apparently no non-exposed group V: NI.	ED EI anti-HAV antibodies	E: 93.4 % (100 % over 50 y) no OR in abstract.	DRR: prevalence von anti-HAV antibodies of 100 % in the "highest occupational risk group"; effect of duration of employment was n.s. Several confounding variables were considered. MA: ?. No further information available in the abstract
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Tornberg and Ronne (1997) ⁴⁸	RS	3790 cases of HA notified between 1980-1995.	notified cases of HA.	average incidence: 4.6/100,000 population per year
Denmark 1980-1995		1980-1995. V: NA.		

* Studies are classified according to strength of their design. General abbreviations are: Md, median; NI: not indicated in the publication; NA: not applicable; n.s.: statistically non-significant; SD: standard deviation.

† Before “year of publication”: indicates that no indication on exact time period could be found

‡ CC: case-control study; CS: cross-sectional study (numbers indicate the rank as described in table 2); HP: historical prospective; RS: reporting scheme.

§ E: exposed; C: controls; population size represents the number of subjects having actually been included (lost cases excluded); age: mean age (range) if not otherwise indicated; M: male; F: female. P: participation rate; R: representativeness of the study population; V: vaccination; “ before 1992”: see methods.

¶ CO: current occupation/job (is mostly a qualitative exposure indicator only); ED: exposure duration in years (mean and range if not otherwise indicated), EI: exposure intensity; EF: exposure frequency.

|| Prevalence: prevalence rates of anti-HAV positive workers. SIR: standardised incidence ratio; OR: adjusted odds ratios and 95 % confidence interval. If no adjusted OR were given crude OR (COR) as reported by the authors are presented. Otherwise, crude ORs (OR^(*)) were calculated on the basis of the data available in the publication (see methods).

“Adjusted” means adjustment for the set of confounding variables considered by the authors. However, the models used for adjustment were not always comparable. If the authors calculated several ORs, all the main ORs are indicated.

** DRR: dose-response relationship; MA: multivariate analysis.