# Hepatitis C virus infection and risk factors in the general population: a large community-based study in eastern China, 2011–2012

P.  $HUANG^{1}$ †, L. G.  $ZHU^{2}$ †, X. J.  $ZHAI^{2}$ , Y. F.  $ZHU^{2}$ , M.  $YUE^{3}$ , J.  $SU^{1}$ , J.  $WANG^{4}$ , H. T.  $YANG^{2}$ , Y.  $ZHANG^{5}$ , H. B.  $SHEN^{1}$ , Z. H.  $PENG^{1*}$  and R. B.  $YU^{1*}$ 

<sup>1</sup>Department of Epidemiology and Biostatistics, School of Public Health, Nanjing Medical University, Nanjing, China

<sup>2</sup> Jiangsu Provincial Centre for Disease Control and Prevention, Nanjing, China

<sup>3</sup> Department of Infectious Diseases, The First Affiliated Hospital of Nanjing Medical University, Nanjing, China

<sup>4</sup>School of Nursing, Nanjing Medical University, Nanjing, China

<sup>5</sup> Department of Epidemiology, Medical Institute of Nanjing Army, Nanjing, China

Received 27 February 2014; Final revision 4 December 2014; Accepted 7 December 2014; first published online 20 January 2015

# SUMMARY

Limited information is available on the prevalence of hepatitis C virus (HCV) in the general population in China. A community-based epidemiological study was conducted in three counties in eastern China. A total of 149 175 individuals were investigated in 60 communities in three counties in Jiangsu province, eastern China, of whom 1175 subjects [0·79%, 95% confidence interval (CI) 0·74–0·83] were HCV antibody positive. The prevalence was low in children (0·09%, 95% CI 0·04–0·17), but increased progressively from adolescents (0·20%, 95% CI 0·15–0·28) to adults aged  $\geq 21$  years (95% CI 0·15–1·64). Women had a higher prevalence of HCV infection than men in most age groups. In a multilevel regression analysis, age, sex, education, occupation, blood transfusion [odds ratio (OR) 2·91, 95% CI 1·09–5·37], invasive testing (OR 1·28, 95% CI 1·14–1·61), and dental therapy (OR 2·27, 95% CI 1·41–3·42) were associated with HCV infection. In conclusion, although the prevalence of HCV in this population was lower than reported from national levels, the total reservoir of infection is significant and warrants public health measures, such as health education to limit the magnitude of the problem.

Key words: Epidemiological study, general population, hepatitis C virus antibody, risk factor.

# INTRODUCTION

Hepatitis C virus (HCV) is a serious public health problem. The global prevalence of HCV infection is about 3%, representing 170 million people worldwide

(Email: rongbinyu@njmu.edu.cn) [Z. H. Peng (Email: rongbinyu@njmu.edu.cn) [R. B. Yu ]

† These authors contributed equally to this work.

[1, 2]. Infection with HCV can cause slowly progressive liver damage that may lead to cirrhosis and/or liver cancer after many decades [3]. Effective therapy, with pegylated interferon and ribavirin, is available and can reduce mortality [4, 5]. China, still a developing country, has a high mortality rate due to hepatocellular carcinoma, and eastern China has a hepatocellular carcinoma mortality rate higher than that of China as a whole [3, 6]. The national prevalence rate in China for antibody HCV (anti-HCV) positivity is  $2 \cdot 20\%$  [7].

<sup>\*</sup> Author for correspondence: Dr Z. H. Peng, Department of Epidemiology and Biostatistics, School of Public Health, Nanjing Medical University, Nanjing 211166, China (Email: zhihangpeng@njmu.edu.cn) [Z. H. Peng]

HCV infection is mainly transmitted by percutaneous exposure to contaminated blood, perinatal exposure from a mother to her infant and unprotected sexual intercourse [2, 3]. The prevalence of HCV infection is higher in high-risk Chinese populations such as drug users (ranging from  $18 \cdot 30\%$  to  $66 \cdot 97\%$ ), and patients undergoing regular dialysis (a pooled prevalence rate of  $41 \cdot 1\%$ ) [8–12]. Although a number of studies on high-risk populations are available, there is a lack of information on the prevalence of HCV infection in the general population. Meanwhile, few studies have reported on the relationship between socioeconomic status and HCV carriage status.

In this study, we planned a population-based serological study to determine the prevalence of anti-HCV in all age groups and to identify possible risk factors for acquiring the infections in eastern China. We hope the findings will eventually guide the development, adaptation, and evaluation of prevention strategies.

# MATERIALS AND METHODS

### Methods

This study was approved by the Institutional Review Board of Nanjing Medical University (Nanjing, China). Planning for this study began in January 2011 and data analysis was completed in December 2012. All field work was conducted from September 2011 to July 2012.

# **Participants**

The target population was local residents in all age groups living in Jiangsu province, eastern China (Fig. 1). These subjects were selected as being representative of the population of eastern China; there was no statistical difference in demographics, the situation of the population or economic conditions between participants in this study and the whole of eastern China. All local residents with >6 months' residency at the time of the survey were selected. A list of residents was obtained from the residents' committee.

# Sampling method

The sample size was calculated as follows:

$$n = \frac{p(1-p)}{\left(\frac{d}{z_{\alpha}}\right)^2} = \frac{z_{\alpha}^2 \times p(1-p)}{d^2},$$

where p is the estimated prevalence rate, d represents power and was calculated by  $0.1 \times p$  and  $z_{\alpha}$  is the statistics of  $\alpha$ . For this study,  $\alpha$  was set at 0.05. Considering the variance of HCV prevalence in different age groups in the survey (0.4% for age <40 years and 1.2% for age  $\geq 40$  years), the desired sample size was 132 534, and included 99 600 young people aged <40 years and 32 934 people aged  $\geq 40$  years.

To represent the entire province's population, a multistage sampling method was used for this study. First, all the provinces were divided into three major regional groups (south, middle, north) where there was a large difference in earnings, education level, and awareness of healthcare and the healthcare system by the inhabitants. One county was randomly selected from each major regional group. As a result, Zhangjiagang, Danyang and Taixing were chosen to represent the south, middle and north sites, respectively (Fig. 1). Second, there were 887 communities in these three counties, and 20 communities were randomly chosen from each county. Finally, all local residents living in the 60 communities for >6 months at the time of the survey were the targeted subjects to be investigated by cluster sampling in this study.

### Investigation

In each community hospital of the 60 communities, there was a survey centre with a team of 20-25 trained staff comprising physicians, nurses, and community doctors to perform the investigation. Before the survey, community doctors issued a letter of physical examination notice to each household on the list of residents. The letter introduced the survey objective, examination items and matters requiring attention. Local residents willing to enrol in the study arrived at the survey centres in the community hospital at the appointed time. A standard questionnaire was used to obtain basic information including gender, birth date, education, occupation, marital status, smoking, drinking, history of hypertension and diabetes, and potential risk factors through a face-to-face interview with the study subject or parent (if the participant was aged <15 years). Definitions of education and occupation were developed according to the Chinese social classification criteria, and were only applicable to the population aged 15-59 years. The occupation of public service worker was defined as a person who works in a hotel, hospital, barbershop, transport centre, etc., and who has high frequency of contact with the public.

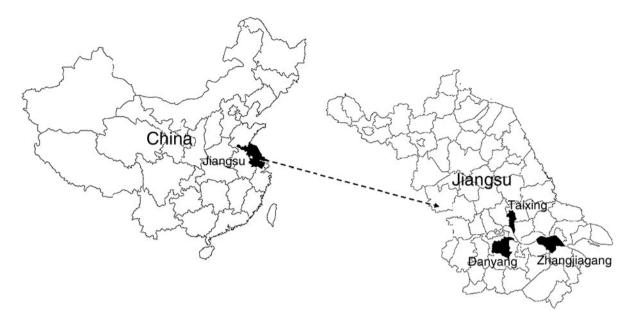


Fig. 1. Map of Jiangsu, eastern China, showing the three counties (black areas) selected for sampling in the study.

## Serological testing

Blood samples collected from each study participant included 5 ml for the population aged >2 years and 2 ml for children aged  $\leq 2$  years or less. Blood samples were collected without anticoagulant and were separated by centrifugation at room temperature. Serum samples were stored at -70 °C. These procedures were completed within 6 h of sample collection. All samples were collected and frozen according to standardized procedures and tested in a central laboratory. Anti-HCV antibodies were detected by enzyme-linked immunoassay with commercial kits (Beijing Wantai Biological Pharmacy Engineering Co. Ltd, China), according to the manufacturer's instructions. Each reaction plate included two negative controls, three positive controls, and one blank control. More than 10% of the samples for which anti-HCV antibody was positive were randomly selected for repeated assays, and the results were 100% concordant.

### Statistical analysis

Differences in demographic characteristics between cases and non-cases were calculated using Student's t test or one-way analysis of variance (for continuous variables) and the  $\chi^2$  test (for categorical variables). The associations of potential risk factors with HCV infection risk were estimated by computing the odds ratios (ORs) and their 95% confidence intervals (CIs) from both univariable and a multivariable

multi-level logistic regression analyses with individuals, communities and counties as the different levels. All statistical analyses were performed with SAS v. 9.1.3 software (SAS Institute Inc., USA), and P < 0.05 in a two-sided test was considered statistically significant.

# RESULTS

### **Basic characteristics**

In this study, 149175 participants was surveyed including 57 188 for Zhangjiagang, 48 422 for Danyang and 43 565 for Taixing. Significant differences were observed for age group in those three counties [mean 37.07 (s.d. = 20.56) years for Zhangjiagang, mean 44.52 (s.d. = 19.77) years for Danyang and mean 45.67 (s.d. = 18.10) years for Taixing; P <0.001]. Distrubution of gender was not different in the three areas. Of the 149 175 subjects studied, 1175 were anti-HCV positive, while the overall prevalence of anti-HCV in this study population was 0.79% (95% CI 0.74-0.83): Zhangjiagang (0.13%, 95% CI 0.11-0.16), Danyang (0.32%, 95% CI 0.27-0.37) and Taixing (2.17%, 95% CI 2.04-2.32). There was a great variation of anti-HCV positivity in the different age groups (Table 1, Fig. 2). The prevalence was low in children (0.09%, 95% CI 0.04-0.17), but increased progressively from adolescents (0.20%, 95% CI 0.15-0.28) to adults aged  $\geq 21$  years (0.15–1.64%). A gender difference was also observed for anti-HCV

Age group, years	Male (no. positive/no. tested), %	Female (no. positive/no. tested), %	Total (no. positive/no. tested), %
≤10	4/5 323 (0.08)	5/4 749 (0. 11)	9/1 0072 (0.09)
11-20	26/1 1093 (0.23)	15/9 044 (0.17)	41/20 137 (0.20)
21-30	8/5 628 (0.14)	11/7 168 (0.15)	19/12 796 (0.15)
31-40	18/9 345 (0.19)	67/13 270 (0.50)	85/22 615 (0.38)
41-50	68/11 508 (0.59)	246/17 256 (1.43)	314/28 764 (1.09)
51-60	142/11 379 (1.24)	274/13 980 (1.96)	416/25 359 (1.64)
61-70	96/8 319 (1.15)	146/9 911 (1.47)	242/18 230 (1.33)
>70	24/4 835 (0.50)	25/6367 (0.39)	49/11 202 (0.44)
All ages	386/67 430 (0.57)	789/81 745 (0.97)	1175/149 175 (0.79)

Table 1. Age- and sex-specific prevalence of anti-HCV in eastern China

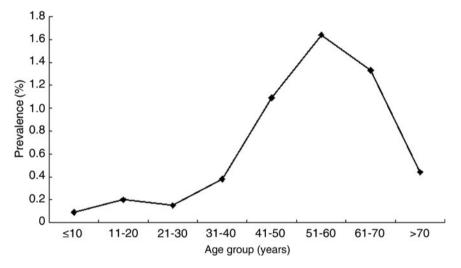


Fig. 2. Age-specific prevalence of anti-HCV in eastern China.

prevalence in participants. Women had a higher prevalence of HCV infection than men in most age groups; the prevalence of anti-HCV was 0.57 (95% CI 0.52-0.63) and 0.97 (95% CI 0.90-1.03) in males and females, respectively (Table 1).

The prevalence of anti-HCV stratified by demographic and selected variables in this study population is described in Table 2. Significant differences were observed for age, sex, marital status, education, occupation, smoking and drinking status and body mass index (BMI) regarding the prevalence of anti-HCV. The prevalence of anti-HCV was higher in participants who were older, heavier, heavier smokers, drinkers or with a previous diagnosis of hypertension or diabetes (P < 0.05 for both comparisons). However, factors such as BMI, and previous diagnosis of hypertension or diabetes might not be truly related to HCV prevalence. Although the sample size of the study was large, any small difference could be detected significantly. HCV prevalence in subjects with a history of hospitalization, surgery, invasive testing, acupuncture, dental therapy and sharing a toothbrush was higher (Table 2).

### **Risk factors**

The frequency of various risk factors associated with HCV infection and the calculated crude OR estimated by univariable analysis are shown in Table 3. Age, sex, marital status, education, occupation, smoking, drinking, BMI, history of hypertension and diabetes, hospitalization, surgery, blood transfusion, invasive test and dental therapy were associated with HCV infection. After adjusting for those variables, older age, female (OR 1·21, 95% CI 1·03–1·34), lower education, agricultural worker, blood transfusion (OR 2·91, 95% CI 1·09–5·37), invasive testing (OR 1·28, 95% CI 1·14–1·61), and dental therapy (OR 2·27, 95% CI

Variables	Anti-HCV negative $(N = 148\ 000), n\ (\%)$	Anti-HCV positive $(N = 1175), n (\%)$	<i>P</i> value
Variables	(N - 148000), h(70)	(1 - 1175), n(70)	I value
Age (years)			
≤10	10 063 (99.91)	9 (0.09)	<0.001
11–20	20 096 (99.80)	41 (0.20)	
21–30	12 777 (99.85)	19 (0.15)	
31-40	22 530 (99.62)	85 (0.38)	
41–50	28 450 (98.91)	314 (1.09)	
51-60	24 943 (98.36)	416 (1.64)	
61–70	17 988 (98.67)	242 (1.33)	
>70	11 153 (99.56)	49 (0.44)	
Sex			<0.001
Male	67 044 (99.43)	386 (0.57)	
Female	80 956 (99.03)	789 (0.97)	
Marital status			<0.001
Unmarried	6714 (99.75)	17 (0.25)	40 001
Married	105 444 (99.00)	1062 (1.00)	
Divorced	6 228 (99·28)	45 (0.72)	
Unknown	442	2	
•	442	Ζ.	<0.001
Education	57.057 (00.00)	(27 (1 10)	<0.001
Primary school	57 057 (98.90)	637 (1·10)	
Middle school	81 485 (99.38)	508 (0.62)	
College school	8704 (99.73)	24 (0.27)	
Unknown	754	6	
Occupation			<0.001
Agricultural worker	39 912 (98.42)	642 (1.58)	
Worker	40 761 (99.28)	294 (0.72)	
Student	29 516 (99.84)	47 (0.16)	
Civil servant	5190 (99.77)	12 (0.23)	
Shop assistant	5274 (99.43)	30 (0.57)	
Unemployed	21 711 (99.48)	114 (0.52)	
Others	4928 (99.44)	28 (0.56)	
Unknown	708	8	
Smoking status	,	0	0.005
Never	115 216 (99.22)	901 (0.78)	0 005
Current	27 003 (99.17)	227 (0.83)	
Past	2699 (98.68)		
Unknown	3082	36 (1·32) 11	
	5082	11	<0.001
Drinking status	100 514 (00 00)	007 (0 70)	<0.001
Never	123 514 (99.28)	897 (0.72)	
Frequently	5902 (98.01)	120 (1.99)	
Every day	2124 (98.97)	22 (1.03)	
Unknown	16 460	136	
Body mass index (kg/m <sup>2</sup> )			
<18.5	18 541 (99.75)	46 (0.25)	<0.001
18.5–24	70 942 (99.19)	576 (0.81)	
24–28	42 987 (98.99)	439 (1.01)	
>28	15 530 (99.27)	114 (0.73)	
<i>P</i> * for trend	× 2	× 2	<0.001
History of hypertension			<0.001
No	127 805 (99.28)	930 (0.72)	
Yes	20 195 (98.80)	245 (1·20)	
History of diabetes	20100 (00 00)	210 (1 20)	0.001
No	145 026 (99.22)	1136 (0.78)	0 001
Yes			
	2974 (98.71)	39 (1.29)	~0.001
Hospitalization	101 479 (00 27)	740 (0.72)	<0.001
No	101 478 (99.27)	749 (0.73)	
Yes	46 522 (99.09)	426 (0.91)	

Table 2. Prevalence of anti-HCV stratified by demographic and selected variables in eastern China

# 2832 P. Huang and others

Tab	le	2	(cont.)	)

	Anti-HCV negative	Anti-HCV positive	
Variables	( <i>N</i> = 148 000), <i>n</i> (%)	( <i>N</i> = 1175), <i>n</i> (%)	P value
Surgery			<0.001
No	115 925 (99.28)	844 (0.72)	
Yes	32 075 (98.98)	331 (1.02)	
Blood transfusion	× ,		<0.001
No	144 839 (99.25)	1095 (0.75)	
Yes	3161 (97.53)	80 (2.47)	
Blood donation	( ),		0.411
No	143 118 (99.21)	1141 (0.79)	
Yes	4882 (99.33)	33 (0.67)	
Invasive testing			<0.001
No	135 049 (99.31)	943 (0.69)	
Yes	12 951 (98.24)	232 (1.76)	
Haemodialysis			0.404
No	147 926 (99.21)	1173 (0.79)	
Yes	174 (99.86)	2 (1.14)	
Acupuncture			<0.001
No	137 970 (99.32)	945 (0.68)	
Yes	10 030 (97.76)	230 (2·24)	
Dental therapy			<0.001
No	115 811 (99.35)	757 (0.65)	
Yes	32 189 (99.17)	418 (1.28)	
Tattoos			0.471
No	147 737 (99.21)	1172 (0.79)	0 171
Yes	263 (98.87)	3 (1.13)	
Piercing		- ()	0.593
No	133 062 (99.22)	1051 (0.78)	0 0,00
Yes	14 938 (99.18)	124 (0.82)	
Sharing needles			0.145
No	147 430 (99.21)	1174 (0.79)	0 1 15
Yes	570 (99.82)	1 (0.18)	
Sharing razors		1 (0 10)	0.153
No	134 572 (99.20)	1083 (0.80)	0 100
Yes	13 428 (99.32)	92 (0.68)	
Sharing toothbrush	10 120 (57 52)	/2 (0 00)	0.011
No	147 477 (99.22)	1165 (0.78)	0 011
Yes	523 (98.12)	10 (1.88)	

\* P value of Cochran–Armitage's trend test.

1.41-3.42) increased the risk of HCV infection (Table 4). All ORs were adjusted by the differences of the three regions.

# DISCUSSION

We report here a community-based epidemiologicak study of HCV infection in an eastern Chinese population with a large sample. This study differs from previous population-based epidemiological studies which mainly had smaller numbers of participants [13–15]. Previous studies on HCV prevalence were mostly derived from high-risk populations such as blood donors, men who have sex with men, and drug users in China and other countries [16–19]. However, owing to the low numbers of elderly and children investigated, these high-risk populations serve as a skewed general population [9]. Meanwhile, in addition to its large number of participants, the present study also used a standardized systematic sampling procedure. As shown in Figure 1, three counties were randomly chosen from three major regional groups as being representative of eastern China. Then 20 communities were randomly selected and each county investigated. In all, 163 462 individuals in 60 communities were identified, and 149 175 participated in

	Unadjusted OR	
Variables	(95% CI)	P value
Age, years		
≤10	1.00	_
11–20	1.38 (1.02-2.61)	0.032
21-30	1.01 (0.62-2.81)	0.615
31–40	3.23 (1.80-7.01)	<0.001
41-50	8.61 (3.09–18.59)	<0.001
51-60	11.85 (5.21-28.04)	<0.001
61–70	12.19 (6.90–21.13)	<0.001
>70	5.21 (1.89-8.09)	<0.001
Sex		0 001
Male	1.00	_
Female	3.19 (1.79–7.10)	<0.001
Marital status	5 15 (1 75 7 10)	\$0.001
Unmarried	1.00	_
Married	4.78 (3.09–7.12)	<0.001
Divorced	1.65 (1.15 - 3.75)	<0.001 <0.001
	1.03(1.13-3.73)	<0·001
Education	1.00	
Primary school	1.00	- 220
Middle school	0.81 (0.52 - 1.32)	0.338
College	0.41 (0.19–0.65)	<0.001
Occupation	1.00	
Agricultural worker	1.00	-
Worker	0.81 (0.59–1.37)	0.418
Student	0.08 (0.03-0.19)	<0.001
Civil servant	0.56 (0.16-0.85)	<0.001
Shop assistant	0.51 (0.34-0.81)	<0.001
Unemployed	0.30 (0.19-0.59)	<0.001
Others	0.46 (0.27-0.73)	<0.001
Smoking		
Never	1.00	-
Current	0.91 (0.78–1.53)	0.469
Past	1.23 (1.05-2.23)	<0.001
Drinking		
Never	1.00	_
Frequently	0.71 (0.48–1.04)	0.078
Every day	1.31 (1.08–1.92)	<0.001
Body mass index (kg/m <sup>2</sup> )		
<18.5	1.00	_
18.5–24	1.57 (1.12–2.93)	<0.001
24–28	2.35(1.89-3.77)	<0.001
>28	3.09(1.67-5.19)	<0.001
History of hypertension	5 05 (1 07 5 15)	40 001
No	1.00	
Yes	1.93 (1.55–2.54)	<0.001
History of diabetes	1 95 (1 55-2 54)	<0.001
No	1.00	
		-
Yes	1.37 (1.15–1.83)	<0.001
Hospitalization	1.00	
No	1.00	-
Yes	1.39 (1.14–1.69)	0.001
Surgery		
No	1.00	_
Yes	1.48 (1.19–1.85)	<0.001

Table 3. Univariable analysis of risk factors associatedwith anti-HCV positivity

Table 3 (cont.)

Unadjusted OR	
(95% CI)	P value
1.00	_
4.05 (2.92-5.63)	<0.001
1.00	—
1.72(0.51-5.63)	0.389
. , ,	
1.00	—
3.13 (2.41-4.23)	<0.001
· · · · ·	
1.00	_
1.01 (0.81 - 1.27)	0.753
1.00	_
1.10 (0.74-1.75)	0.681
1.00	_
3.11 (1.76-4.46)	<0.001
1.00	_
1.96 (0.96-4.79)	0.069
1.00	_
0.62(0.35-1.21)	0.612
1.00	_
1.03 (0.71 - 1.48)	0.587
1.00	_
0.67 (0.45-1.09)	0.128
1.00	_
	0.431
	(95%  CI) $1.00$ $4.05 (2.92-5.63)$ $1.00$ $1.72 (0.51-5.63)$ $1.00$ $3.13 (2.41-4.23)$ $1.00$ $1.01 (0.81-1.27)$ $1.00$ $1.01 (0.74-1.75)$ $1.00$ $3.11 (1.76-4.46)$ $1.00$ $1.96 (0.96-4.79)$ $1.00$ $0.62 (0.35-1.21)$ $1.00$ $1.03 (0.71-1.48)$ $1.00$ $0.67 (0.45-1.09)$

OR, Odds ratio; CI, confidence interval.

the survey. This sampling procedure was aimed at eliminating bias from local social, economic or cultural factors that might be associated with the prevalence of HCV. However, there are clear issues with representativeness, as the sample is highly likely to underrepresent injecting drug users (IDUs). IDUs are difficult to survey and fail to appear in this survey, which inevitably leads to an underestimate of the true prevalence of the general population. However, this is a common problem in most population-based surveys [20, 21].

This community-based study in eastern China found an anti-HCV seroprevalence of 0.79% (95% CI 0.74-0.83), which was much lower than the reported average national prevalence (2.20%) [7]. Because local living conditions are high, well above

Variables	aOR (95% CI)	P value
Age, years		
≤10	1.00	-
11–20	1.12 (0.78–1.87)	0.413
21-30	0.93 (0.33-3.18)	0.894
31-40	1.65 (0.61-7.92)	0.276
41–50	2.16 (1.05-9.19)	<0.001
51-60	3.25 (1.67–12.14)	0.003
61–70	1.44 (1.12-5.08)	<0.001
>70	1.04 (0.41–9.13)	0.615
Sex		
Male	1.00	_
Female	1.21 (1.03–1.34)	<0.001
Marital status		
Unmarried	1.00	-
Married	0.88 (0.48–1.62)	0.818
Divorced	1.08 (0.45–1.91)	0.436
Education		
Primary school	1.00	—
Middle school	0.76 (0.51–1.80)	0.716
College	0.61 (0.45–0.97)	0.003
Occupation		
Agricultural worker	1.00	-
Worker	1.05 (0.72–1.92)	0.562
Student	0.31 (0.11–0.62)	<0.001
Civil servant	0.71 (0.24–1.02)	0.074
Shop assistant	0.82 (0.63–1.02)	0.062
Unemployed	0.52 (0.43–0.80)	<0.001
Others	0.68 (0.51–1.31)	0.341
Smoking		
Never	1.00	_
Current	1.31 (0.92–2.17)	0.337
Past	1.17 (0.89–1.43)	0.213
Drinking	1.00	
Never	1.00	-
Frequently	0.98 (0.62 - 1.12)	0.187
Every day	1.22 (0.69–1.24)	0.538
Body mass index (kg/m <sup>2</sup> )	1.00	
<18.5	1.00	-
18·5–24	1.31 (0.84 - 2.01)	0.298
24–28 >28	1.04 (0.59-1.25) 0.94 (0.51-1.21)	0·514 0·623
History of hypertension	0.94 (0.31–1.21)	0.025
No	1.00	
Yes	1.10(0.91 - 1.29)	0.081
History of diabetes	1 10 (0 91–1 29)	0 081
No	1.00	
Yes	1.00 1.05 (0.73 - 1.42)	0.482
Hospitalization	1 05 (0 75-1 42)	0 402
No	1.00	_
Yes	0.73 (0.51 - 1.12)	0.632
Surgery	0 / 5 (0 51-1 12)	0.052
No	1.00	_
Yes	1.00 1.04 (0.61 - 1.31)	 0·564
Blood transfusion	107(001-151)	0 304
No	1.00	_
110	1.00	

Table 4. Multivariable analysis of risk factorsassociated with anti-HCV positivity

Table 4 (cont.)

Variables	aOR (95% CI)	P value
Yes	2.91 (1.09-5.37)	<0.001
Invasive testing		
No	1.00	_
Yes	1.28 (1.14-1.61)	<0.001
Dental therapy		
No	1.00	_
Yes	2.27 (1.41-3.42)	<0.001
Tattoos		
No	1.00	_
Yes	1.02 (0.95-3.82)	0.105

aOR, Adjusted odds ratio; CI, confidence interval.

the national average, the healthcare system is welldeveloped in this region. Moreover, as residents in this study are well-educated and have a good awareness of healthcare, they have a healthy lifestyle which helps minimize the risk of HCV infection.

Age-specific prevalence of HCV in our study was low in children (0.09%), but increased progressively from adolescents (0.20%) to adults aged  $\geq 21$  years (0.15-1.64%). For subjects aged between 41 and 70 years, anti-HCV prevalence was much higher than for the younger groups. One of the most important reasons for this is that the elderly may have an increased risk of exposure to HCV infection such as multiple injections and a shortage of healthcare resources. In addition, with the improvement of healthcare, nosocomial infections through inadequately sterilized equipment, transplantation, and iatrogenic transmission by blood transfusion have reduced [22]. However, considering the many HCVrelated hepatocellular carcinoma deaths in the >70 years age group, it is very reasonable that HCV prevalence was low in that group. The increasing anti-HCV seroprevalence with advanced age observed in this study was concordant with that found in previous study in China [22]. However, there is an interesting phenomenon in that the prevalence in those aged 21-30 years is less than in those aged 11-20 years. The reason may be that IDUs who are mainly in the 21-30 years age group were reluctant to participate in this survey, which may lead to an underestimation of the true prevalence in those aged 21–30 years. Another interesting phenomenon is that there are significantly fewer participants in the 21-30 years age group. There are two possible reasons why fewer young individuals participated in this study. First, is that people aged 21-30 years usually live or work in

big cities such as Shanghai. Few of these individuals return to their home town. The second reason may be that this group has less interest in this type of survey than older age groups. Therefore, the 21–30 years age group is always likely to be underrepresented.

Women had a higher prevalence of HCV infection than men in this study, which differs from previous studies in Western countries but is in accord with previous surveys of six regions of China and Taiwan [15, 22]. One of the main reasons for this may be that IDUs are generally more likely to be male, but this group is difficult to survey and does not appear in this study, leading to an underestimation of the true prevalence of males. Second, unlike Western countries, the practice of commercial plasma donation led to a high prevalence of HCV infections in China in the 1980s [23]. During that period women in rural areas were the main donors, which may explain the prevalence of HCV in females being much higher than in males aged 41-70 in this survey. However, pursuant to the Law for Donating Blood being issued in 1998, blood transfusions and the use of serumrelated products have become safer in recent years in China [24]. There was no such difference in the prevalence of HCV between males and females aged <40 years. In the >70 years age group, anti-HCV prevalence in females was lower, which may be because many HCV-related cirrhosis and hepatocellular carcinoma patients had died. Finally, obstetric measures were one important way of contracting HCV infection due to lack of healthcare in past decades [15].

In our study mixed-effects logistic regression revealed that blood transfusion, invasive testing and dental therapy increased the risk of HCV infection. A history of blood transfusions in particular was the greatest risk factor for HCV infection in this investigation. This may be associated with commercial plasma donation in rural areas of China in the 1980s [23]. For invasive testing and dental therapy, the main reason was that due to lack of systematic training programmes physicians were unable to understand HCV and sterilization procedures well enough in some underdeveloped villages. Moreover, in the past the general population had less education regarding healthcare and lacked knowledge regarding HCV transmission. Therefore, health education for the general population, especially the elderly, is very important, and may prove to be useful in preventive interventions in China [25].

A major limitation of this study is that lack of HCV RNA level information hinders the ability to identify individuals with persistent HCV infection and those requiring care and treatment, leading to a failure to control the spread of the virus. However, it is fairly well-established that about 25% of individuals spontaneously clear acute HCV infection, meaning that 75% of HCV infections persist [26]. According to the observed prevalence of antibodies in this study, an estimate of chronic prevalence is 0.59% (95% CI 0.55-0.63) [20]. As HCV genotypes were not tested in this study, it is difficult to explore the introduction, spread and evolution of HCV. Furthermore, we performed the simple sampling first, which may have caused bias in estimating the total prevalence of the whole province, i.e. the rate of 0.79% (95% CI 0.74-0.83) is probably narrow. Although the three counties are selected randomly, they represent three different regions which may have huge differences in living standards. Finally, the inclusion of so much risk information in the survey, may have induced a potential recall bias in this study.

Despite these limitations, this study is the first to investigate HCV infection with such a large general population utilizing a standardized systematic sampling method. Even with a lower prevalence of HCV infection, there may be millions of potential persons at risk of cirrhosis and hepatocellular carcinoma due to HCV. The epidemiological data in the present investigation may play an important role in focusing on the significance of public health in chronic HCV infection. As no vaccine exists currently for HCV, health education should be further strengthened to limit the spread of HCV infections.

# **ACKNOWLEDGEMENTS**

We thank the students who have worked on the study, including Yingying Zhu, Qing Wang, Hui Zheng, Yuanyuan Zhang, Yin Xu, Wenzhe Ma. We also thank the staff from the Centers for Disease Control and Prevention of Jiangsu province for organization of the field investigation. This research would not have been possible without the consent and help of the participants.

This study was supported in part by National Natural Science Foundation of China (No. 81273146, No. 81001288 and No. 81473029), National S&T Major Project Foundation of China (No. 2011ZX10004-902 and No. 2012ZX10001-001), Priority Academic Program Development of Jiangsu Higher Education Institutions (PAPD), Jiangsu Province Health Development Project with Science and Education (No. ZX201109), National Science and Technology Support Program (No. 2011BAI09B02)), and Research and Innovation Project for College Graduates of Jiangsu Province of China (KYZZ\_0265).

# **DECLARATION OF INTEREST**

None.

# REFERENCES

- 1. Lavanchy D. Chronic viral hepatitis as a public health issue in the world. *Best Practice & Research Clinical Gastroenterology* 2008; 22: 991–1008.
- Shepard CW, et al. Global epidemiology of hepatitis C virus infection. Lancet Infectious Diseases 2005; 5: 558–567.
- El-Serag HB. Epidemiology of viral hepatitis and hepatocellular carcinoma. *Gastroenterology* 2012; 142: 1264– 1273.e1261.
- 4. **Muir AJ**, *et al*. Phase 1b study of pegylated interferon lambda 1 with or without ribavirin in patients with chronic genotype 1 hepatitis C virus infection. *Hepatology* 2010; **52**: 822–832.
- Asselah T, et al. Hepatitis C: viral and host factors associated with non-response to pegylated interferon plus ribavirin. *Liver International* 2010; 30: 1259–1269.
- Bruix J, Sherman M. Management of hepatocellular carcinoma: an update. *Hepatology* 2011; 53: 1020–1022.
- Lavanchy D. Evolving epidemiology of hepatitis C virus. *Clinical Microbiology and Infection* 2011; 17: 107–115.
- Zhou YH, et al. Comparison of HIV-, HBV-, HCV- and co-infection prevalence between Chinese and Burmese intravenous drug users of the China-Myanmar border region. PLoS ONE 2011; 6: e16349.
- 9. Nelson PK, et al. Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews. *Lancet* 2011; **378**: 571–583.
- Su Y, et al. Prevalence and risk factors of hepatitis C and B virus infections in hemodialysis patients and their spouses: A multicenter study in Beijing, China. *Journal of Medical Virology* 2013; 85: 425–432.
- Ruan Y, et al. Evaluation of harm reduction programs on seroincidence of HIV, Hepatitis B and C, and syphilis among intravenous drug users in southwest China. Sexually Transmitted Diseases 2013; 40: 323–328
- 12. Patel PR, et al. Epidemiology, surveillance, and prevention of Hepatitis C virus infections in hemodialysis

patients. American Journal of Kidney Diseases 2010; 56: 371–378.

- Charlebois A, et al. Factors associated with HCV antiviral treatment uptake among participants of a community-based HCV programme for marginalized patients. Journal of Viral Hepatitis 2012; 19: 836–842.
- Cozzolongo R, et al. Epidemiology of HCV infection in the general population: a survey in a southern Italian town. American Journal of Gastroenterology 2009; 104: 2740–2746.
- 15. Lee M-H, *et al.* Community and personal risk factors for hepatitis C virus infection: a survey of 23 820 residents in Taiwan in 1991–2. *Gut* 2011; **60**: 688–694.
- Ng M-H, et al. High prevalence but low awareness of hepatitis C virus infection among heroin users who received methadone maintenance therapy in Taiwan. Addictive Behaviors 2013; 38: 2089–2093.
- van der Helm J, et al. Effect of HCV infection on causespecific mortality after HIV seroconversion, before and after 1997. Gastroenterology 2013; 144: 751–760.e752.
- Bao YP, Liu ZM. Systematic review of HIV and HCV infection among drug users in China. *International Journal of STD & AIDS* 2009; 20: 399–405.
- Dai S, et al. Seroprevalence of HIV, syphilis, and hepatitis C virus in the general population of the Liangshan Prefecture, Sichuan Province, China. Journal of Medical Virology 2012; 84: 1–5.
- De Angelis D, et al. An evidence synthesis approach to estimating Hepatitis C prevalence in England and Wales. Statistical Methods in Medical Research 2009; 18: 361–379.
- Hickman M, et al. Injecting drug use in Brighton, Liverpool, and London: best estimates of prevalence and coverage of public health indicators. *Journal of Epi*demiology and Community Health 2004; 58: 766–771.
- 22. Lu J, *et al.* General epidemiological parameters of viral hepatitis A, B, C, and E in six regions of China: a cross-sectional study in 2007. *PLoS ONE* 2009. 4: e8467.
- Rao HY, et al. Outcome of hepatitis C virus infection in Chinese paid plasma donors: a 12–19-year cohort study. *Journal of Gastroenterology and Hepatology* 2012; 27: 526–532.
- Lu F, Zhuang H. Prevention of hepatitis B in China: achievements and challenges. *Chinese Medical Journal* (*English*) 2009; 122: 2925–2927.
- Mitchell AE, et al. Institute of medicine recommendations for the prevention and control of hepatitis B and C. *Hepatology* 2010; 51: 729–733.
- 26. Micallef JM, Kaldor JM, Dore GJ. Spontaneous viral clearance following acute hepatitis C infection: a systematic review of longitudinal studies. *Journal of viral hepatitis* 2006; **13**: 34–41.