

The prevalence and influencing factors of hepatitis B among rural resident population in Zhejiang province

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1 Title: The prevalence and influencing factors of hepatitis B among rural resident population in
2 Zhejiang province

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45 **ABSTRACT**

46 **Objectives** In order to reveal the prevalence among rural resident population and associated
47 influencing factors of hepatitis B, so as to help developing specific control strategies.

48 **Methods** We conducted a cross-sectional study among rural resident population in Zhejiang,
49 China. 16601 participants were sampled from five districts. Univariate and multivariate analysis
50 was applied to evaluate the influencing factors. Odds ratios of each related factor were assessed
51 with or without adjustment separately.

52 **Results** The age of participants was 40.28 ± 19.47 , and there were 7881 males and 8720 females.
53 The positive rate of hepatitis B surface antigen (HBsAg) was 4.04% (95% CI: 3.74%-4.35%) and
54 it was 3.85% by age and gender standardized. Univariate analysis showed that age, education level,
55 occupation, live status, taken examinations, history of blood transfusion, vaccination, family
56 history, hepatitis B surface antibody (HBsAb), being coastal and district were the potential
57 influencing factors. Multivariate logistic model indicated that occupation, living status, history of
58 examination, vaccination, HBsAb and district were the influencing factors. Undertaking a service
59 based tertiary industry job ($OR_a=1.33$, 95% CI: 1.04-1.69), non-single live ($OR_a=2.66$, 95% CI:
60 2.04-3.46) were the risk factors, while having taken examinations ($OR_a=0.68$, 95% CI: 0.47-0.99),
61 vaccinated ($OR_a=0.52$, 95% CI: 0.41-0.65) and HBsAb positive ($OR_a=0.11$, 95% CI: 0.08-0.15)
62 were the protective factors.

63 **Conclusions** Hepatitis B is an intermediate epidemic level in rural resident, with a rate of 3.85%.
64 Enlarging the population of screening, raising the coverage of vaccination especially in adults are
65 suitable strategies to prevention and control of hepatitis B among rural resident population.

66 **Keywords:** Hepatitis B; Influencing factors; Cross-sectional study

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67 **ARTICLE SUMMARY**

68 **Strengths and limitations of this study**

69 This study focused on the prevalence of hepatitis B among rural resident population.

70 The study involved large rural resident population and the logistic regression model provided a
71 quantified result of influencing factors of hepatitis B.

72 The main limitation of the study was there could be recall bias, for its cross-sectional designed.
73

74 **INTRODUCTION**

75 Hepatitis B is a potentially life-threatening liver infection caused by hepatitis B virus (HBV),
76 which attacks the liver and could cause both acute and chronic disease. Two billion people have
77 evidence of past or present infection with HBV, and an estimated 240 million people are
78 chronically infected with hepatitis B virus globally[1-2]. More than 686000 people die annually
79 due to complications of hepatitis B, including cirrhosis and hepatocellular carcinoma (HCC)[3].

80 Previously study revealed that the incidence of HBV-related HCC in adults remains high, and high
81 serum HBV DNA level increases the risks of cirrhosis and HCC[4-5].

82 Overall, almost half of global population live in areas of high hepatitis B endemicity[6]. Global
83 prevalence of HBV infection is heterogeneous[2], the prevalence of hepatitis B is highest in
84 sub-Saharan Africa and East Asia, where 5%~10% of the adult population is chronically
85 infected[1]. A nearest large nationwide survey in China was conducted in 2006, and which showed
86 that the weighted prevalence of hepatitis B surface antigen (HBsAg) positive was 7.2% among
87 aged 1~59 years and the rate among children aged <5 years was only 1.0%[7]. According to the
88 endemicity maps[2], hepatitis B in China was at a higher intermediate level. From then on, several

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4 89 studies[8-14] had been conducted to investigate the prevalence of hepatitis B in different areas
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6 90 among general population in mainland China. The reported rate was 3.49% in Beijing (2007)[8],
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9 91 4.38% in adults in Northeast China (2007)[9], 7.44% in Anhui province (2006)[10], 5.17% in
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11 92 Henan Province (2006~2009)[11], 7.2% in Northwest China (2010)[12] and 3.17% in Sichuan
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13 93 blood donors (2010~2011)[13] and 2.73% in Beijing (2013~2014)[14]. The values of rate were
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15 94 varied in different areas and time periods.
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19 95 It is important issue to identify the prevalence of hepatitis B, and it is the basic procedure on the
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21 96 way of eradicating HBV infection. This study aimed to investigate the prevalence of hepatitis B
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23 97 and its potential influencing factors among rural resident population in Zhejiang province, China.
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25 98 By indicating the epidemic of hepatitis B and its associated risk factors clearly in rural areas, we
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27 99 could develop specific prevention and control strategies based on the influencing factors of HBV
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29 100 infection and characteristic endemic of hepatitis B.
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35 36 102 **METHODS**

37 38 103 **Study design**

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40 104 A stratified multistage cluster sampling survey was conducted in five districts in Zhejiang
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42 105 province, China from January 2014 to December 2015. Three organization levels of stratification
43
44 106 sampling were involved: districts, rural town and villages. All participants were rural resident
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46 107 registered and those who had continuously living at local for at least six months were included.
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49 108 During the two-year planed investigation, a standard questionnaire was designed for the
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51 109 cross-sectional survey and was used to collect basic information of the rural resident participants
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53 110 and the potential factors for HBV infection.
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4 111 A house-to-house investigation was completed by trained staffs and local doctors at sampled areas.
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6 112 In order to increase the response rate, staffs were recommended to visit target house at appropriate
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9 113 time period like nightfall. One percent questionnaire will be randomly checked after the survey
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11 114 each time. Basic personal information was collected, including age, gender, ethnicity, education,
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13 115 occupation, marital status, medical insurance, history of hepatitis B examination, history of blood
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15 116 transfusion, history of surgery, history for being out 3 months, vaccination history of hepatitis B,
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17 117 family history of hepatitis B and whether living in coastal. And these data were carried out by
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19 118 staffs with face-to-face interviews.
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24 119 Serum were collected from blood samples (5 ml for individuals aged ≥ 6 years old and 2 ml for
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26 120 children aged ≤ 5 years old) and stored at -20°C by laboratory staffs from the local hospitals.
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29 121 Serum were timely shipped to our state key laboratory of the First Affiliated Hospital, College of
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31 122 Medicine, Zhejiang University. Serum samples were tested by chemiluminescence immunoassay
32
33 123 (CLIA) with Abbott reagents centralized. We considered the positive rate of HBsAg among
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35 124 population as the level of hepatitis B prevalence.
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38 39 125 **Statistical analysis**

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41 126 All collected data was entered into an EpiData 3.1 software database twice. Then we checked the
42
43 127 accuracy, consistency and logical of the data. SAS 9.4 (SAS Institute Inc., Cary, NC) software was
44
45 128 used for data processing and analysis. Social demographic information was performed by
46
47 129 descriptive statistics. Univariate logistic analysis was used to identify potential influencing factors
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49 130 associated with hepatitis B infection, we selected the factor with $P < 0.1$ in univariate model and
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51 131 conducted a stepwise multivariate logistic model to seek the independent risk factors for hepatitis
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55 132 B. Odds ratio (OR), 95% confidence interval (95% CI) and adjusted OR for each factor were also
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4 133 calculated. The statistical hypothesis test level was 0.05. GraphPad Prism 6.0 (GraphPad Software,
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6 134 Inc., La Jolla, CA) was used to draw the figures.
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136 **RESULTS**

137 **Characteristics of participants**

138 A total of 16601 participants were interviewed including 7881 (47.47%) males and 8720 (52.53%)
139 females in five districts. The age of participants was 40.28 ± 19.47 years old. The prevalence of
140 hepatitis B among whole participants was 4.04% (95% CI: 3.74%-4.35%), and it was 3.85%
141 standardized by age and gender with demographic population of Zhejiang province. It showed that
142 Zhejiang was an intermediate epidemic area of hepatitis B.

143 The distribution of population and prevalence rate between different age groups were showed in
144 Figure 1. We could see that age below 20 years were the groups which had lowest prevalence rate
145 of hepatitis B, while groups aged 41~60 years had highest rate. There was a rapid increase of
146 prevalence rate between aged 21~25 years and 26~30 years.

147 Among the five districts, Shaoxing had the most participants with a number of 5416 (32.65%),
148 while Yuhuan had the smallest number with 1447 (8.72%) participants. The numbers of
149 participants in rest Putuo, Tonglu and Tongxiang districts were 4370 (26.32%), 3523 (21.22%)
150 and 1845 (11.11%), separately. The prevalence of hepatitis B was highest in Yuhuan (9.81%),
151 and lowest in Tongxiang (2.49%) in our study (Figure 2).

152 We collected all the concerned data of participants, basic characteristics of the participants were
153 listed in Table 1. Most of the participants' education level was primary school or lower (44.25%),
154 college or higher level was only 1088 (6.55%) and in which group had the lowest prevalence

155 (2.21%). Only 13.48% of the participants had taken hepatitis B examination before. Few ones
 156 had a history of surgery (3.46%) or blood transfusion (0.57%). There were 6358 (38.30%)
 157 participants had a vaccination history of hepatitis B, and it was 75.5% in aged <20 years old,
 158 while it was only 29.8% in aged >20 years old. Of all participants, 5817 (35.04%) were living
 159 in coastal areas. HBsAb positive rate was 30.00%, and among which HBsAg positive rate was
 160 only 1.00%, the value was lower than that in HBsAb negative ones (5.34%).

161
 162 Table 1 The characteristics of participants in the study and results of univariate analysis

Variables/Values	Sample		HBsAg	
	size	Percent	positive	Prevalence
	(n)	(%)	(n)	(%)
Age**	16601	-	670	4.04
Gender				
Male	7881	47.47	324	4.11
Female	8720	52.53	346	3.97
Education level**				
Primary school or lower	7346	44.25	305	4.15
Junior school	5431	32.71	265	4.88
High or polytechnic school	2736	16.48	76	2.78
College or higher	1088	6.55	24	2.21
Occupation**				
Agriculture based primary industry	5862	35.31	256	4.37

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4	Manufacturing based second industry	623	3.75	39	6.26
5					
6	Service based tertiary industry	2423	14.60	132	5.45
7					
8	Others (Students or retired)	7693	46.34	243	3.16
9					
10					
11	Living status**				
12					
13	Single live	5299	31.92	81	1.53
14					
15	Non-single live	11302	68.08	589	5.21
16					
17					
18					
19	Medical insurance				
20					
21	Self-pay	339	2.04	13	3.83
22					
23					
24	Have medical insurance	16262	97.96	657	4.04
25					
26	History of hepatitis B examination*				
27					
28	Yes	2238	13.48	71	3.17
29					
30	No	14363	86.52	599	4.17
31					
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34	History of surgery**				
35					
36	Yes	575	3.46	48	8.35
37					
38	No	16026	96.54	622	3.88
39					
40					
41	History of blood transfusion				
42					
43	Yes	94	0.57	4	4.26
44					
45	No	16507	99.43	666	4.03
46					
47					
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49	Vaccination history of hepatitis B**				
50					
51	Yes	6358	38.30	122	1.92
52					
53	No	10243	61.70	548	5.35
54					
55					
56	History for being out 3 months				
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Yes	843	5.08	39	4.63
No	15758	94.92	631	4.00
Family history of hepatitis B**				
Yes	446	2.69	69	15.47
No	16155	97.31	601	3.72
Living in coastal**				
Yes	5817	35.04	296	5.09
No	10784	64.96	374	3.47
HBsAb**				
Negative	11621	70.00	620	5.34
Positive	4980	30.00	50	1.00
District**				
Putuo	4370	26.32	154	3.52
Shaoxing	5416	32.62	197	3.64
Tonglu	3523	21.22	131	3.72
Tongxiang	1845	11.11	46	2.49
Yuhuan	1447	8.72	142	9.81

163 *: P < 0.05; **: P < 0.0001.

164

165 Univariate and multivariate analysis

166 Univariate analysis showed that age, educational level, occupation, living status, history of

167 hepatitis B examination, vaccination history of hepatitis B, history of surgery, history for

168 being out 3 months, family history of hepatitis B, living in coastal, HBsAb and district could
 169 be the potential influencing factors associated with hepatitis B among general population
 170 (Table 1).

171 A stepwise multivariate analysis showed that occupation, living status, history of hepatitis B
 172 examination, vaccination history of hepatitis B, HBsAb and district were the independent
 173 influencing factors of hepatitis B among rural resident population in Zhejiang. An age and
 174 gender adjusted model revealed that undertaking a service based tertiary industry job
 175 ($OR_a=1.33$, 95% CI: 1.04-1.69), non-single live ($OR_a= 2.66$, 95% CI: 2.04-3.46) were the risk
 176 factors for hepatitis B prevalence, while taken an examination of hepatitis B ($OR_a= 0.68$, 95%
 177 CI: 0.47-0.99), hepatitis B vaccinated ($OR_a= 0.52$, 95% CI: 0.41-0.65) and HBsAb positive
 178 ($OR_a= 0.11$, 95% CI: 0.08-0.15) were the protective factors for hepatitis B (Table 2). Figure 3
 179 illustrated the values of OR and OR_a in the two logistic models.

181 Table 2 Results of multivariate analysis for hepatitis B

Variables/Values	OR (95% CI)	<i>P</i> value	OR_a (95% CI)	<i>P</i> value
Occupation				
Agriculture based primary industry	ref.		ref.	
Manufacturing based second industry	1.17(0.80-1.71)	0.4259	1.14(0.78-1.68)	0.5034
Service based tertiary industry	1.35(1.07-1.71)	0.0124	1.33(1.04-1.69)	0.0236

Others	0.73(0.60-0.90)	0.0029	0.73(0.59-0.89)	0.0026
Living status				
Single live	ref.		ref.	
Non-single live	2.59(2.02-3.33)	<0.0001	2.66(2.04-3.46)	<0.0001
History of hepatitis B examination				
Yes	0.68(0.47-0.99)	0.0459	0.68(0.47-0.99)	0.0456
No	ref.		ref.	
Vaccination history of hepatitis B				
Yes	0.52(0.42-0.66)	<0.0001	0.52(0.41-0.65)	<0.0001
No	ref.		ref.	
HBsAb				
Positive	0.11(0.08-0.15)	<0.0001	0.11(0.08-0.15)	<0.0001
Negative	ref.		ref.	
District				
Putuo	ref.		ref.	
Shaoxing	0.81(0.65-1.02)	0.0714	0.81(0.65-1.02)	0.0690
Tonglu	0.67(0.51-0.88)	0.0045	0.67(0.51-0.88)	0.0047
Tongxiang	0.28(0.19-0.39)	<0.0001	0.28(0.20-0.40)	<0.0001
Yuhuan	4.15(3.19-5.39)	<0.0001	4.15 (3.19-5.40)	<0.0001

182 OR: odds ratio; OR_a: odds ratio adjusted by age and gender; ref.: reference.

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6 186 Viral hepatitis is a leading cause of death and disability worldwide, deaths from acute infection,
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8 187 cirrhosis and liver cancer were the tenth leading cause worldwide in 1990, while it ranked seventh
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10 188 in 2013. And the number of deaths worldwide attributable to viral hepatitis increased by 63% from
11
12 189 1990 to 2013[15]. World Health Organization (WHO) adopted the first-ever global hepatitis
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14 190 strategy with a goal to eliminate viral hepatitis B and C as a public health threat by 2030, defined
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16 191 as a reduction in incidence by 90% in new chronic infections and mortality by 65% of viral
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18 192 hepatitis B and C[16]. Hepatitis B is a major health problem and a significant socio-economic
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20 193 impact all over the world currently[17].
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22 194 China has the world's largest rural population and labor[18], rural population flow is a main
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24 195 component of China's population flow and has an important impact on the spatial pattern of
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26 196 population on regional economic and social development[19]. A hepatitis B prevalence of 3.7%
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28 197 (642) of a large sample was reported previously[20], while it was 6% (124274) tested positive for
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30 198 HBsAg among males in rural areas by another study[21]. Rural economy lags behind the city in
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32 199 China, along with the resource and level of health or education. Vaccination coverage related to
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34 200 the economy status, former study suggested that higher HBV vaccination coverage rates among
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36 201 adults are obtainable and user fees, time needed of vaccination and travel costs had acted as
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38 202 economic barriers to vaccination[22]. The vaccination of hepatitis B was reported as low as
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40 203 13.89% in rural China[23].
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42 204 The prevalence of hepatitis B among whole rural resident participants was 4.04% in Zhejiang (It
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44 205 was 3.85% standardized by age and gender). Which indicated that Zhejiang rural resident
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46 206 population would be categorized as an intermediate group, and the prevalence rate of hepatitis B
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4 207 was significantly lower than reported 9.8% in 1992 and 7.2% in 2006 across inland China[7].

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6 208 Following a series of interventions by the Chinese government, there was a significantly decline

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9 209 of the hepatitis B epidemic. A larger nation-wide survey would be needed to assess the epidemic

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11 210 of hepatitis B in China in order to provide the epidemiological features and update the controlling

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14 211 or preventing strategies, especially in rural population.

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16 212 There was no significantly association between hepatitis B prevalence and age in our study.

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19 213 Although previous studies referred age as a factor[24-27], and showed that an older age caused a

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21 214 higher prevalence in population. Our univariate analysis also indicated this phenomena. We

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24 215 thought it was a result of confounding by hepatitis B vaccination or other factors. A former study

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26 216 reported a reverse result too[28]. For the factor of gender, the results were varied. Studies[11, 25,

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29 217 28-30] showed that the prevalence rate was higher in male than in female ones, while there was no

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31 218 association founded between gender and hepatitis B by a study[24] just like ours did.

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34 219 Our study showed that education was not an independent influencing factor on hepatitis B, while

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36 220 other studies pointed this out[31-32]. But there could be a possible trend that hepatitis B

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39 221 prevalence decreasing with increasing of education level from univariate analysis and Table 1,

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41 222 higher education level in our study had a lower rate of hepatitis B prevalence. Potential reasonable

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44 223 explanations for this phenomena were: Well prevention or protection awareness of infectious

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46 224 diseases like hepatitis B in higher educated population; A higher acceptance of vaccination, having

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49 225 at least a college education (OR= 2.55, 95% CI: 1.28-5.07) was an important predictor of vaccine

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51 226 completion[33].

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54 227 We found that only 13.48% in whole had taken hepatitis B examinations before and among those

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57 228 participants had a lower prevalence of hepatitis B, while those who had not been examined existed

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4 229 a higher prevalence rate. We could infer that those infected by hepatitis B virus who had not been
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6 230 diagnosed by the examinations could be the potential sources of hepatitis B. By encouraging
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9 231 people to take part in hepatitis B examination along with routine physical examination, we could
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11 232 benefit: First, we could find out those infected one; Second, we could treat them immediately;
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14 233 Third, it could be the right opportunity to raise awareness of hepatitis B among population
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16 234 especial in rural areas.
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19 235 Service based tertiary industry of occupation seemed to be a risk factor compared to other ones,
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21 236 non-single live ($OR_a = 2.66$, 95% CI: 2.04-3.46) were the risk factors for hepatitis B prevalence.
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24 237 Above factors had the same feature: it likely to result in more communications between people.
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26 238 We should take consideration of these since hepatitis B is an infectious disease and has a sign of
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29 239 clustering among population.
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31 240 Epidemics of hepatitis B were scattered in different areas globally[2, 27], prevalence rates of
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34 241 hepatitis B among districts were also varied in our study. This circumstance would be caused by
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36 242 geographic, economic level, density of the population, living habits or other factors. Regardless of
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39 243 all these, we should take district as a non-negligible factor especially district with a high
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41 244 prevalence like Yuhuan (9.81%) when develop and implement strategies fighting for hepatitis B.
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44 245 Chinese government had made great progresses with vaccination for hepatitis B[34], the national
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46 246 hepatitis B immunization plan was established in 1992. In 2002, the Global Alliance on Vaccine
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49 247 and Immunization (GAVI) partnered with the government of China to provide hepatitis B vaccine
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51 248 for free[35]. And fully integrated into the routine immunization program and provided completely
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54 249 free among infants nationally in 2005[36]. The carrier rate in Chinese children aged <5 years fell
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57 250 to less than 1% in 2006, and 0.32% in 2014, which was 10% in the 1990s[37]. Recently data from
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4 251 WHO estimated of newborns in China receive a timely birth dose (TBD) and third dose of
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6 252 hepatitis B vaccine (HepB3) were 96% and 99% respectively[38]. Our study shows that Hepatitis
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9 253 B vaccinated ($OR_a = 0.52$, 95% CI: 0.41-0.65) and HBsAb positive ($OR_a = 0.11$, 95% CI: 0.08-0.15)
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11 254 were the protective factors for hepatitis B, same results had been observed[12-13, 31].
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14 255 Our sampled survey showed the vaccination rate was 75.5% in aged <20 years old, while it was
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16 256 only 29.8% in aged >20 years old. There was a trend that rate of hepatitis B vaccination was
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19 257 increased when the vaccination program conducted and expanded since 1992, along with the
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21 258 decreasing of hepatitis B prevalence nationwide. Preventing hepatitis B through vaccine is
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24 259 currently the most efficient way to decrease HBV-related cirrhosis and liver cancer incidence, as
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26 260 well as to suppress the HBV reservoir[17]. The role of the vaccination program for effective
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29 261 control of hepatitis B should be emphasized[39]. In the near future, we should focus on adults
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31 262 about hepatitis B vaccination under the consideration of policies for universal vaccination delayed,
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34 263 especially in countries with high endemicity.
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39 265 **CONCLUSIONS**

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41 266 In conclusion, though our study showed Zhejiang rural area is categorized as an intermediate
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43 267 epidemic level in China, it is still an important issue and big challenge to deal with the problem of
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46 268 hepatitis B in rural areas among resident population. Specific methods like enlarging the
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49 269 population of hepatitis B examination, raising the coverage of vaccination particularly in adults
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51 270 are considered as suitable and effective strategies to prevention and control of hepatitis B in
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54 271 Zhejiang rural areas.

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273 **LIMITATION**

274 This study was cross-sectional designed, there was a certain of recall bias. We excepted to control
275 it at a low level during design and conduct periods. Sample sizes seemed not so balanced between
276 districts in our study. We considered taking a vaccination history of hepatitis B as vaccine success,
277 for the effectiveness of vaccination[17]. In order to interpreter the results, we simply divided
278 variables into few groups like occupation. A more precise classification of factors could be
279 involved in later studies, along with much more potential factors associated with hepatitis B.

280

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282 The funders had no role in study design, data collection, data analysis or writing of the report. The
283 corresponding author had full access to all the data in the study, and had final responsibility for the
284 decision to submit for publication.

285 **Footnotes**

286 SY and CD contributed equally.

287 **Contributors**

288 LL, JR, BR, JY and SY conceived and designed the study. CD, YC, JW, CY, CP, KX, MD, YL, JL,
289 PY, WR, YQ, QC and YZ collected data, cleaned, analyzed the data and revised the paper. CD and
290 SY wrote the first draft of the paper, contributed to figures and paper preparation and all authors
291 critically revised the paper and gave final approval for publication.

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5
6 296 self-research project of State Key Laboratory for Diagnosis and Treatment of Infectious Diseases,
7
8
9 297 The First Affiliated Hospital, College of Medicine, Zhejiang University, China].

10
11 298 **Competing interests**

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13
14 299 None declared.

15
16 300 **Ethics approval**

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19 301 This study was approved by the Ethics Committee of the First Affiliated Hospital, College of
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21 302 Medicine, Zhejiang University and consent was obtained from all participants.

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23 303 **Data sharing statement**

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26 304 No additional data are available.

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333 [ines.pdf](http://www.worldhepatitisalliance.org/sites/default/files/resources/documents/Hep%20B%20Guidelines.pdf) (accessed 10 Oct 2016).
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54 425 Figure 1 The prevalence of hepatitis B among different age groups
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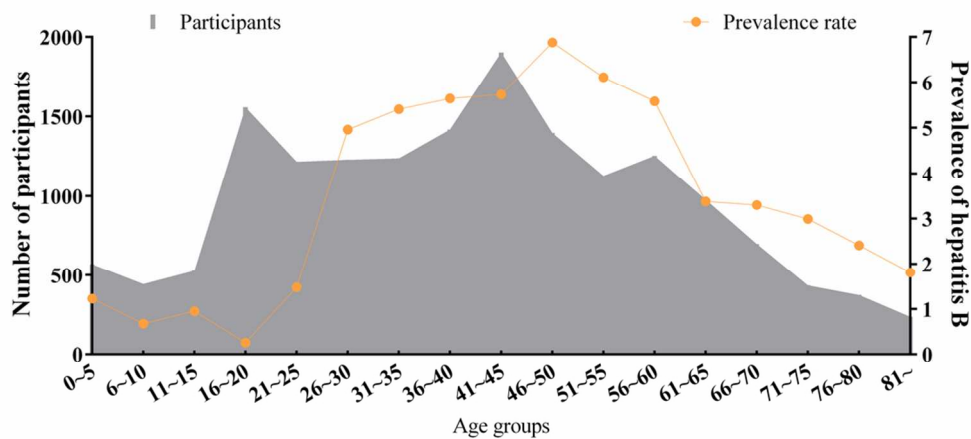
56 426 Figure 2 The distribution of participants and prevalence of hepatitis B in different districts
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427 Figure 3 The values of OR and OR_a in the logistic models.

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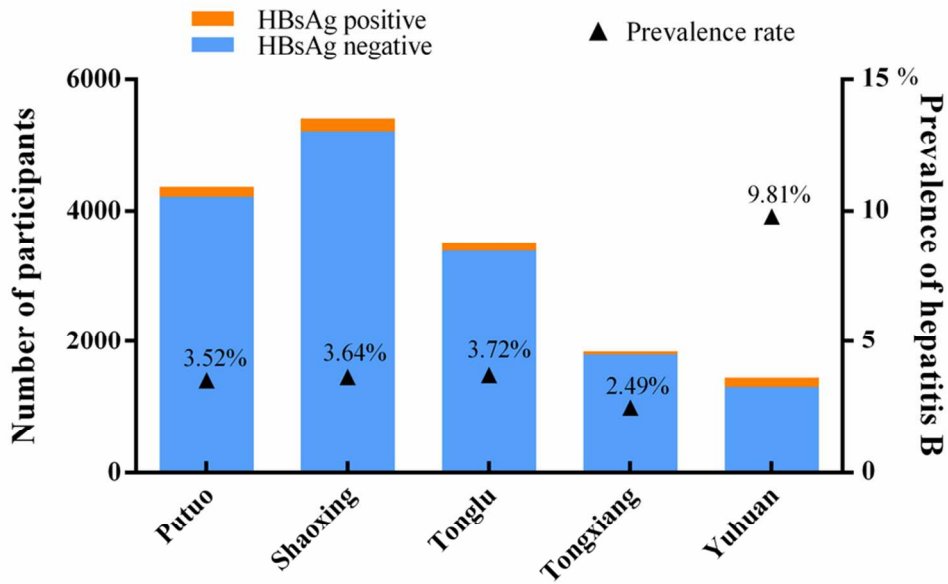
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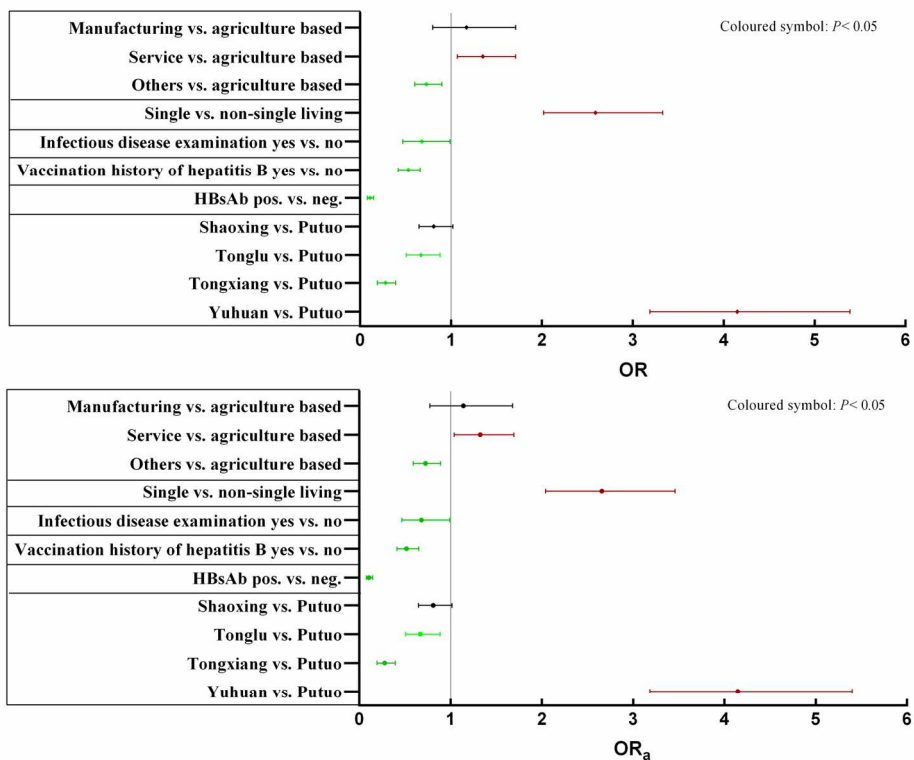
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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	3
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	18
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6,9
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	6
		(b) Describe any methods used to examine subgroups and interactions	
		(c) Explain how missing data were addressed	
		(d) If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest	7,8,9 7
Outcome data	15*	Report numbers of outcome events or summary measures	7
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	9-12
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	13-15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	16
Generalisability	21	Discuss the generalisability (external validity) of the study results	16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

The prevalence and influencing factors of hepatitis B among a rural residential population in Zhejiang Province, China: a cross-sectional study

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1 Title: The prevalence and influencing factors of hepatitis B among a rural residential population in
2 Zhejiang Province, China: a cross-sectional study

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45 **ABSTRACT**

46 **Objectives** To reveal the prevalence and associated influencing factors of hepatitis B among a
47 rural residential population in Zhejiang, China to help developing specific control strategies.

48 **Methods** We conducted a cross-sectional study among a rural residential population in Zhejiang,
49 China. Stratified multistage cluster sampling was utilized in five districts, questionnaires were
50 completed by trained local staffs and all data were collected. Then univariate and multivariate
51 analyses were applied to evaluate the influencing factors. The odds ratios of each related factor
52 were assessed with or without adjustment separately.

53 **Results** The mean age of the 16601 participants who completed the survey was 40.28 ± 19.47
54 years, and there were 7881 males and 8720 females. The positive rate of hepatitis B surface
55 antigen (HBsAg) was 4.04% (95% CI: 3.74%-4.35%), it was 3.85% standardized by age and
56 gender. Univariate analysis showed that age, educational level, occupation, living status,
57 examinations taken, history of blood transfusion, vaccination, family history, being coastal, and
58 district were the potential influencing factors. Multivariate logistic regression indicated that
59 occupation, living status, history of examination, vaccination and district were the influencing
60 factors. Undertaking a service-based tertiary industry job ($OR_a=1.19$, 95% CI: 0.94-1.51) and
61 non-single living ($OR_a=2.84$, 95% CI: 2.17-3.70) might be risk factors, while vaccinated
62 ($OR_a=0.43$, 95% CI: 0.34-0.53) and having taken examinations ($OR_a=0.71$, 95% CI: 0.48-1.03)
63 were potential protective factors.

64 **Conclusions** Hepatitis B is at an intermediate epidemic level in a rural residential population in
65 Zhejiang, China, with a prevalence rate of 3.85%. Raising vaccination coverage, especially in
66 adults, is a suitable strategy for the prevention and control of hepatitis B in a rural residential

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4 67 population in Zhejiang, China.

5
6 68 **Keywords:** Hepatitis B; Influencing factors; Cross-sectional study

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9 69 **ARTICLE SUMMARY**

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11 70 **Strengths and limitations of this study**

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14 71 This study focused on the prevalence of hepatitis B in a rural residential population.

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16 72 The study involved a large rural residential population and the logistic regression model provided
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18 73 a quantified result of the influencing factors of hepatitis B.

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21 74 The main limitation of the study was that there could be recall bias due to its cross-sectional
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23 75 design.

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29 77 **INTRODUCTION**

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31 78 Hepatitis B is a potentially life-threatening liver infection caused by hepatitis B virus (HBV),
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33 79 which attacks the liver and could cause both acute and chronic disease. Two billion people have
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35 80 evidence of past or present HBV infection, and, globally, an estimated 240 million people are
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37 81 chronically infected with hepatitis B virus [1 2]. More than 686000 people die annually due to
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39 82 complications of hepatitis B, including cirrhosis and hepatocellular carcinoma (HCC)[3].

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42 83 Previously, studies revealed that the incidence of HBV-related HCC in adults remains high, and a
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44 84 high serum HBV DNA level increases the risks of cirrhosis and HCC[4 5].

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47 85 Overall, nearly half of the global population lives in areas of high hepatitis B endemicity[6]. The
48
49 86 global prevalence of HBV infection is heterogeneous[2], and the prevalence of hepatitis B is the
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51 87 highest in sub-Saharan Africa and East Asia, where 5%~10% of the adult population is chronically
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53 88 infected[1]. The most recent large, nationwide survey in China was conducted in 2006, which
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4 89 showed that the weighted prevalence of hepatitis B surface antigen (HBsAg) positive was 7.2%
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6 90 among those aged 1 to 59 years, and the rate among children aged <5 years was only 1.0%[7].
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9 91 According to the endemicity maps[2], hepatitis B in China was at a higher intermediate level.
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11 92 Since that time, several studies[8-14] have been conducted to investigate the prevalence of
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13 93 hepatitis B in different areas among the general population in mainland China. The reported
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15 94 prevalence rate was 3.49% in Beijing (2007)[8], 4.38% in adults in Northeast China (2007)[9],
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17 95 7.44% in Anhui Province (2006)[10], 5.17% in Henan Province (2006-2009)[11], 7.2% in
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19 96 Northwest China (2010)[12], 3.17% in Sichuan blood donors (2010-2011)[13] and 2.73% in
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21 97 Beijing (2013-2014)[14]. The values of rate were varied in different areas and time periods.
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26 98 China has the world's largest rural population and labor resources[15], and the rural population
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28 99 flow is a main component of China's population flow and has an important impact on the spatial
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31 100 pattern of the population in terms of regional economic and social development[16]. A hepatitis B
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33 101 prevalence of 3.7% (642) in a large sample was previously reported[17]; while this figure was 6%
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35 102 (124274) among males in rural areas who tested positive for HBsAg by another study[18]. The
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37 103 rural economy lags behind the urban economy in China, along with the resources, health and
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39 104 education levels.
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44 105 It is important issue to identify the prevalence of hepatitis B and the basic procedure for
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46 106 eradicating HBV infection. This study aimed to investigate the prevalence of hepatitis B and its
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48 107 potential influencing factors in a rural residential population in Zhejiang Province, China. By
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50 108 clearly indicating the epidemic of hepatitis B and its associated risk factors in rural areas, we
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52 109 could develop specific prevention and control strategies based on the influencing factors of HBV
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54 110 infection and the characteristics of hepatitis B endemic.
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6 112 **METHODS**7
8 113 **Study design**

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11 114 A survey with stratified multi-stage cluster sampling survey was conducted in five districts in
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14 115 Zhejiang Province, China from January 2014 to December 2015. We took geographic
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16 116 characteristics and economic levels into consideration when choosing the five districts in our study,
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18 117 coastal areas such as Putuo and Yuhuan, inland areas such as Shaoxing, Tonglu, and Tongxiang,
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21 118 higher economic level areas such as Shaoxing and Tongxiang, and lower economic level areas
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23 119 such as Putuo, Yuhuan and Tonglu. Further stratified sampling was based on the population in
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25 120 rural town and villages. All participants, who were registered rural residents and had been
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27 121 continuously living at the local for at least six months were included.

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31 122 During the two-year planned investigation, a standard questionnaire was designed for the
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33 123 cross-sectional survey and was used to collect basic information about the rural residential
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35 124 participants and the potential factors for HBV infection.

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38 125 A house-to-house investigation was completed by trained staffs and local doctors in the sampled
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40 126 areas. To increase the response rate, staffs were recommended to visit target houses at an
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42 127 appropriate time period, such as nightfall. One percent of the questionnaires were randomly
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44 128 checked, each time, after conducting the survey. Basic personal information was collected,
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46 129 including age, gender, ethnicity, education, occupation, living status, medical insurance, history of
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48 130 hepatitis B examination, history of blood transfusion, history of surgery, history of being away 3
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50 131 months, vaccination history of hepatitis B, family history of hepatitis B, and whether living in a
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52 132 coastal area. These data were collected by staffs in face-to-face interviews.
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4 133 Sera were collected from blood samples (5 ml for individuals aged ≥ 6 years and 2 ml for
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6 134 children aged ≤ 5 years) and stored at -20 °C by laboratory staffs from the local hospitals. Sera
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9 135 were timely shipped in a timely manner to our state key laboratory of the First Affiliated Hospital,
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11 136 College of Medicine, Zhejiang University. Serum samples were tested by chemiluminescence
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13 137 immunoassay (CLIA) with Abbott reagents (Abbott Laboratories, Abbott Park, IL, USA). We
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15 138 considered the positivity rate of HBsAg in the population as the prevalence level of hepatitis B.

19 139 **Statistical analysis**

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21 140 All collected data were entered into an EpiData 3.1 software database twice. Then, we checked the
22
23 141 accuracy, consistency and logistics of the data. SAS 9.4 (SAS Institute Inc., Cary, NC, USA)
24
25 142 software was used for data processing and analysis. Social demographic information was analysed
26
27 143 by descriptive statistics. Univariate logistic analysis was used to identify potential influencing
28
29 144 factors associated with hepatitis B infection; we selected the factors with $P < 0.1$ in the univariate
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31 145 model and conducted a stepwise multivariate logistic model to seek the independent risk factors
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33 146 for hepatitis B. Odds ratio (OR), 95% confidence interval (95% CI) and adjusted OR for each
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35 147 factor were also calculated. The statistical hypothesis test level was 0.05. GraphPad Prism 6.0
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37 148 (GraphPad Software, Inc., La Jolla, CA, USA) was used to draw the figures.
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46 150 **RESULTS**

48 151 **Characteristics of participants**

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51 152 Of the 22000 eligible participants, 16601 completed the survey with a response rate of 75.5%,
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53 153 including 7881 (47.47%) males and 8720 (52.53%) females in five districts. The mean age of the
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55 154 participants was 40.28 ± 19.47 years. The prevalence of hepatitis B in all participants was 4.04%

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4 155 (95% CI: 3.74%-4.35%), and it was 3.85% when standardized by age and gender, using the
5
6 156 demographic population of Zhejiang Province as the standard population. The results showed that
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9 157 Zhejiang was an intermediate epidemic area of hepatitis B.

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11 158 The distribution of the population and the prevalence rate between the different age groups are
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14 159 shown in Figure 1. We can observe that an age below 20 years is the group that had the lowest
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16 160 prevalence rate of hepatitis B, while groups aged 41-60 years had the highest rates. There was a
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19 161 rapid increase in the prevalence rate between those aged 21-25 years and 26-30 years.

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21 162 Among the five districts, Shaoxing had the most participants with a number of 5416 (32.65%),
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24 163 while Yuhuan had the smallest number with 1447 (8.72%) participants. The numbers of
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26 164 participants in the rest of the areas, Putuo, Tonglu and Tongxiang districts, were 4370
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29 165 (26.32%), 3523 (21.22%) and 1845 (11.11%), respectively. In our study, the prevalence of
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31 166 hepatitis B was highest in Yuhuan (9.81%), and lowest in Tongxiang (2.49%) in our study
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34 167 (Figure 2).

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36 168 We collected all the relevant data of the participants; participant's basic characteristics are listed in
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38
39 169 Table 1. Most of the participants' educational level was primary school or lower (44.25%), college
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41 170 level or higher was only 1088 (6.55%), and the group, which had the lowest prevalence (2.21%).
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44 171 Only 13.48% of the participants had undergone hepatitis B examination before, and few had a
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46 172 history of surgery (3.46%) or blood transfusion (0.57%). There were 6358 (38.30%)
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48
49 173 participants, who had a vaccination history of hepatitis B, and this figure was 75.5% for aged
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51 174 <20 years, and only 29.8% in aged >20 years. Of all participants, 5817 (35.04%) were living
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54 175 in coastal areas and the HBsAb positive rate was 30.00%, and among which the HBsAg

176 positive rate was only 1.00%, a value that was lower than that in HBsAb negative participants

177 (5.34%).

178

179 Table 1 Characteristics of participants in the study and univariate analysis results

Variables/Values	Sample		HBsAg	
	size	Percent	positive	Prevalence
	(n)	(%)	(n)	(%)
Age**	16601	-	670	4.04
Gender				
Male	7881	47.47	324	4.11
Female	8720	52.53	346	3.97
Educational level**				
Primary school or lower	7346	44.25	305	4.15
Junior school	5431	32.71	265	4.88
High or polytechnic school	2736	16.48	76	2.78
College or higher	1088	6.55	24	2.21
Occupation**				
Agriculture-based primary industry	5862	35.31	256	4.37
Manufacturing-based secondary industry	623	3.75	39	6.26
Service-based tertiary industry	2423	14.60	132	5.45
Other (Students or retired)	7693	46.34	243	3.16

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4	Living status**				
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6	Single living	5299	31.92	81	1.53
7					
8	Non-single living	11302	68.08	589	5.21
9					
10					
11	Medical insurance				
12					
13	Out-of-pocket	339	2.04	13	3.83
14					
15	Has medical insurance	16262	97.96	657	4.04
16					
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18					
19	History of hepatitis B examination*				
20					
21	Yes	2238	13.48	71	3.17
22					
23	No	14363	86.52	599	4.17
24					
25					
26	History of surgery**				
27					
28	Yes	575	3.46	48	8.35
29					
30	No	16026	96.54	622	3.88
31					
32					
33					
34	History of blood transfusion				
35					
36	Yes	94	0.57	4	4.26
37					
38	No	16507	99.43	666	4.03
39					
40					
41	Vaccination history of hepatitis B**				
42					
43	Yes	6358	38.30	122	1.92
44					
45	No	10243	61.70	548	5.35
46					
47					
48					
49	History for being away 3 months				
50					
51	Yes	843	5.08	39	4.63
52					
53	No	15758	94.92	631	4.00
54					
55					
56	Family history of hepatitis B**				
57					
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Yes	446	2.69	69	15.47
No	16155	97.31	601	3.72
Living in coastal area**				
Yes	5817	35.04	296	5.09
No	10784	64.96	374	3.47
HBsAb				
Negative	11621	70.00	620	5.34
Positive	4980	30.00	50	1.00
District**				
Putuo	4370	26.32	154	3.52
Shaoxing	5416	32.62	197	3.64
Tonglu	3523	21.22	131	3.72
Tongxiang	1845	11.11	46	2.49
Yuhuan	1447	8.72	142	9.81

180 *: P < 0.05; **: P < 0.0001.

181

182 Univariate and multivariate analysis

183 Univariate analysis showed that age, educational level, occupation, living status, history of
 184 hepatitis B examination, vaccination history of hepatitis B, history of surgery, history for
 185 being away 3 months, family history of hepatitis B, and living in a coastal area and district
 186 could be the potential influencing factors associated with hepatitis B among the population
 187 (Table 1).

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4 188 A stepwise multivariate analysis showed that occupation, living status, history of hepatitis B
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6 189 examination, vaccination history of hepatitis B and district were the independent influencing
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9 190 factors of hepatitis B in a rural residential population in Zhejiang. An age and gender adjusted
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11 191 model revealed that undertaking a service-based tertiary industry job ($OR_a=1.19$, 95% CI:
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13 192 0.94-1.51), non-single living ($OR_a=2.84$, 95% CI: 2.17-3.70) were the risk factors for
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15 193 hepatitis B prevalence; while having taken an examination of hepatitis B ($OR_a=0.71$, 95% CI:
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17 194 0.48-1.03) and hepatitis B vaccinated ($OR_a=0.43$, 95% CI: 0.34-0.53) might be the protective
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19 195 factors for hepatitis B (Table 2). Figure 3 illustrates the values of OR and OR_a in the two
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21 196 logistic models.
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29 198 Table 2 Results of multivariate analysis for hepatitis B

Variables/Values	OR (95% CI)	<i>P</i> value	OR_a (95% CI)	<i>P</i> value
Occupation				
Agriculture-based primary industry	ref.		ref.	
Manufacturing-based secondary industry	1.26(0.87-1.82)	0.2155	1.18(0.82-1.72)	0.3857
Service-based tertiary industry	1.25(1.00-1.58)	0.0548	1.19(0.94-1.51)	0.1586
Other	0.79 (0.65-0.97)	0.0237	0.77(0.63-0.94)	0.0113
Living status				
Single living	ref.		ref.	

Non-single living	2.63(2.05-3.37)	<0.0001	2.84(2.17-3.70)	<0.0001
History of hepatitis B examination				
Yes	0.72(0.49-1.04)	0.0787	0.71(0.48-1.03)	0.0705
No	ref.		ref.	
Vaccination history of hepatitis B				
Yes	0.45(0.36-0.56)	<0.0001	0.43(0.34-0.53)	<0.0001
No	ref.		ref.	
District				
Putuo	ref.		ref.	
Shaoxing	0.77(0.62-0.97)	0.0236	0.77(0.62-0.96)	0.0208
Tonglu	0.79(0.60-1.05)	0.1031	0.79(0.60-1.05)	0.1025
Tongxiang	0.38(0.27-0.53)	<0.0001	0.38(0.27-0.54)	<0.0001
Yuhuan	2.09(1.63-2.67)	<0.0001	2.09(1.63-2.67)	<0.0001

199 OR: odds ratio; OR_a: odds ratio adjusted by age and gender; ref.: reference.

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202 DISCUSSION

203 Prevalence of hepatitis B

204 Viral hepatitis is a leading cause of death and disability worldwide, deaths from acute infection,
 205 cirrhosis and liver cancer were the tenth leading cause of death worldwide in 1990, while it ranked
 206 seventh in 2013. The number of deaths worldwide attributable to viral hepatitis increased by 63%
 207 from 1990 to 2013[19].

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4 208 The prevalence of hepatitis B in all rural residential participants was 4.04% in Zhejiang (It was
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6 209 3.85% standardized by age and gender). Our results indicated that the Zhejiang rural residential
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9 210 population would be categorized as an intermediate group and that the hepatitis B prevalence rate
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11 211 was significantly lower than reported in 1992 of 9.8% and in 2006 of 7.2% across inland China[7].
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14 212 Following a series of interventions by the Chinese government, there was a significantly decline
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16 213 of the hepatitis B epidemic. A larger nation-wide survey would be needed to assess the current
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18 214 epidemic of hepatitis B in China to provide the epidemiological features and update the
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20 215 controlling or prevention strategies, especially in the rural population.
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22

23 24 216 **Influencing factors of hepatitis B**

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26 217 There was no significantly association between hepatitis B prevalence and age in our study.
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29 218 Although, previous studies referred to age as a factor[20-22], and showed that an older age group
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31 219 had a higher prevalence in the population. Our univariate analysis also indicated this phenomenon.
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34 220 We thought this outcome was a result of confounding, by hepatitis B vaccination or other factors.
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36 221 A former study also reported an inverse result[23]. For the factor of gender, the results were varied.
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39 222 Previous studies[11 21 23-25] showed that the prevalence rate was higher in males than in females;
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41 223 while there was no association founded between gender and hepatitis B in one study[20] similar to
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44 224 our own.
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46 225 Our study showed that education was not an independent influencing factor on hepatitis B; while
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49 226 other studies also notes this[26 27]. However, there could be a possible trend of decreasing
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51 227 hepatitis B prevalence with increasing educational level from our univariate analysis in Table 1; it
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54 228 can be observed in our study that higher educational level had a lower rate of hepatitis B
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56 229 prevalence rate. Potential reasonable explanations for these phenomena are better prevention or
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4 230 protection awareness of infectious diseases, such as hepatitis B, in the higher-educated population
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6 231 and a higher acceptance of vaccination; furthermore, having at least a college education (OR=2.55,
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9 232 95% CI: 1.28-5.07) was an important predictor of vaccine completion[28].

10
11 233 We found that only 13.48% of all participants had taken a hepatitis B examinations before, and
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13 234 among those participants, there was a lower prevalence of hepatitis B; while in those participants
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16 235 who had not been previously examined, there was a higher prevalence rate. We could infer that
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18 236 those infected by hepatitis B virus, who had not been diagnosed by the examinations, could be the
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21 237 potential sources of hepatitis B. By encouraging people to take part in hepatitis B examination,
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24 238 along with routine physical examination, we could benefit: First, we could find out those who are
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26 239 infected; Second, we could immediately treat them; Third, the right opportunity could exist to
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29 240 raise awareness of hepatitis B among the population, especially in rural areas.

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31 241 Compared to other occupation types, service-based tertiary industry of occupation seemed to be a
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34 242 risk factor, along with non-single living (OR_a=2.84, 95% CI: 2.17-3.70), which were the risk
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36 243 factors for hepatitis B prevalence. The factors above had the same feature: likely to result in more
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39 244 communications between people. We should take consideration of these factors, since hepatitis B
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41 245 is an infectious disease, which has a sign of clustering among the population.

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43
44 246 Hepatitis B epidemics are scattered in different areas globally[2 22], and hepatitis B prevalence
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46 247 rates also varied among the districts in our study. These circumstances would be caused by
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49 248 geography, economic level, population density, living habits or other factors. Economic level
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51 249 seems to be a potential factor, since lower economic level areas such as Yuhuan had a higher
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54 250 prevalence rate and higher areas such as Shaoxing and Tongxiang had prevalence lower rates.

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56 251 Regardless of all features, we should consider district as a non-negligible factor, especially a
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4 252 district with a high prevalence, when developing and implementing strategies for fighting hepatitis

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9 254 **Control strategies for hepatitis B**

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11 255 World Health Organization (WHO) adopted the first-ever global hepatitis strategy with a goal to

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13 256 eliminate viral hepatitis B and C as public health threats by 2030, which was defined as a

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15 257 reduction in incidence by 90% in new chronic infections and mortality by 65% for viral hepatitis

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17 258 B and C[29]. Currently, hepatitis B is a major health problem and has a significant socio-economic

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19 259 impact all over the world currently[30]. HBV vaccination is the mainstay of HBV prevention and

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21 260 it is the most effective prevention strategy[31 32].

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23 261 The Chinese government has made great progresses with hepatitis B vaccination[33]: the national

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25 262 hepatitis B immunization plan was established in 1992. In 2002, the Global Alliance on Vaccine

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27 263 and Immunization (GAVI) partnered with the government of China to provide free hepatitis B

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29 264 vaccine[34] and fully integration into the routine immunization program, and the vaccine was

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31 265 provided completely free to infants, nationally in 2005[35]. The carrier rate in Chinese children

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33 266 aged <5 years fell to less than 1% in 2006, and 0.32% in 2014, which previously was 10% in the

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35 267 1990s[36]. Recently, WHO estimated that new-borns in China, who received a timely birth dose

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37 268 (TBD) and third dose of hepatitis B vaccine (HepB3), was 96% and 99% respectively[37]. Our

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39 269 study shows that Hepatitis B vaccination ($OR_a=0.43$, 95% CI: 0.34-0.53) was the protective

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41 270 factors for hepatitis B, and the same results have previously been observed[12 13 26].

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43 271 Regarding vaccination coverage related to the economy status, a former study suggested that

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45 272 higher HBV vaccination coverage rates among adults are obtainable and that user fees, time

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47 273 needed for vaccination and travel costs acted as economic barriers to vaccination[38]. Hepatitis B

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4 274 vaccination has been reported as low as 13.89% in rural China[39]. We call for strengthening
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6 275 HBV vaccination in rural areas, and raising the vaccine coverage rate.
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9 276 Our survey also showed that the vaccination rate was 75.5% in aged <20 years, and was only 29.8%
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11 277 in aged >20 years. There was a trend that the rate of hepatitis B vaccination was increased when
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13 278 the vaccination programme conducted and expanded since 1992, along with decreasing
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15 279 nationwide hepatitis B prevalence. Preventing hepatitis B through vaccination is currently the
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17 280 most efficient way to decrease HBV-related cirrhosis and liver cancer incidence and reduce the
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19 281 HBV reservoir[30]. The role of the vaccination programme for the effective control of hepatitis B
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21 282 should be emphasised[40]. In the near future, we should focus hepatitis B vaccination efforts on
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23 283 adults, under the consideration of policies for delayed universal vaccination, especially in
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25 284 countries with high endemicity.
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34 286 **CONCLUSIONS**

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36 287 In conclusion, though our study showed that the Zhejiang rural area is categorized as an
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38 288 intermediate epidemic level for hepatitis B in China, there remains the important issue and
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40 289 formidable challenge of dealing with the problem of hepatitis B in rural areas among the resident
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42 290 population. Specific methods such as raising the coverage of vaccination particularly in adults, are
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44 291 suitable and effective strategies to prevent and control hepatitis B in Zhejiang rural areas.
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46 292 Furthermore, increasing the percentage of the population that has had hepatitis B examination may
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48 293 also be considered as a potential strategy.
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55 295 **LIMITATION**

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4 296 This study was cross-sectionally designed, and we could not exclude the acute infection case; thus
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6 297 the hepatitis B prevalence rate may be overestimated in the population when using the HBsAg
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9 298 positive rate as the level of chronic HBV infection, and there was also a certainty of recall bias in
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11 299 this study design. Additionally, the sample sizes were not balanced between districts in our study.
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14 300 We considered taking a vaccination history of hepatitis B as an indicator of vaccine success due to
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16 301 the effectiveness of vaccination[30]. To interpret the results, we simply divided the variables
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19 302 into few groups, such as occupation. A more precise classification of factors could be assessed in
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21 303 later studies, along with other more potential factors, such as family income.
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29 306 The funders had no role in study design, data collection, data analysis or writing of the report. The
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31 307 corresponding author had full access to all the data in the study and had the final responsibility for
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33
34 308 the decision to submit for publication.

309 **Footnotes**

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39 310 SY and CD contributed equally.

311 **Contributors**

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44 312 LL, JR, BR, JY and SY conceived and designed the study. CD, YC, JW, CY, CP, KX, MD, YL, JL,
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46 313 PY, WR, YQ, QC and YZ collected data, cleaned, and analysed the data and revised the paper. CD
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48
49 314 and SY wrote the first draft of the paper, contributed to figures and paper preparation and all
50
51 315 authors critically revised the paper and gave final approval for publication.

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6 319 [National Natural Science Foundation of China] grant number [81001271, 81672005], [the key
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13 322 Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital,
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15 323 College of Medicine, Zhejiang University, China] [2016KF11].

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19 324 **Competing interests**

20
21 325 None declared.

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24 326 **Ethics approval**

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26 327 This study was approved by the Ethics Committee of the First Affiliated Hospital, College of
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28 328 Medicine, Zhejiang University and consent was obtained from all participants.

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31 329 **Data sharing statement**

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33 330 No additional data are available.

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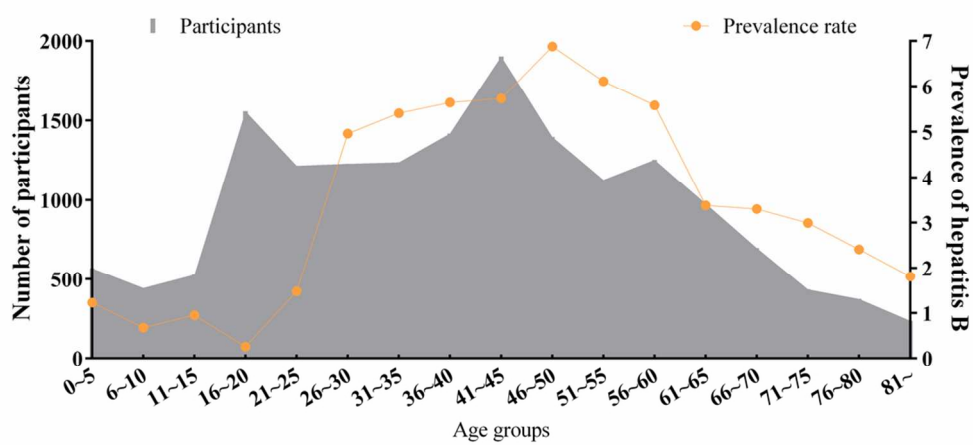
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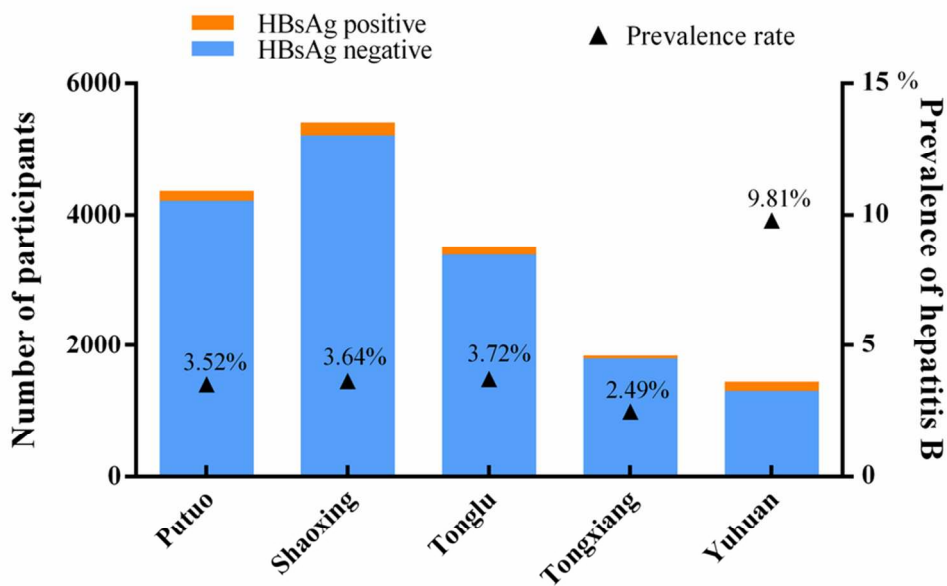
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24 458 Figure 1 The prevalence of hepatitis B among different age groups
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26 459 Figure 2 The distribution of participants and prevalence of hepatitis B in different districts
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29 460 Figure 3 The values of OR and OR_a in the logistic models.
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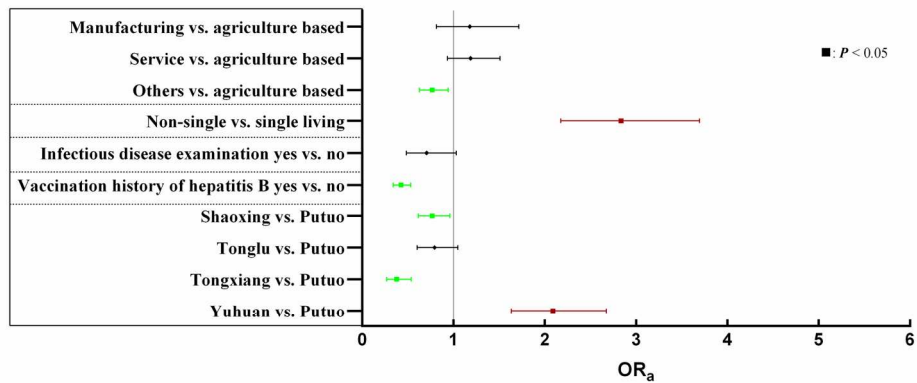
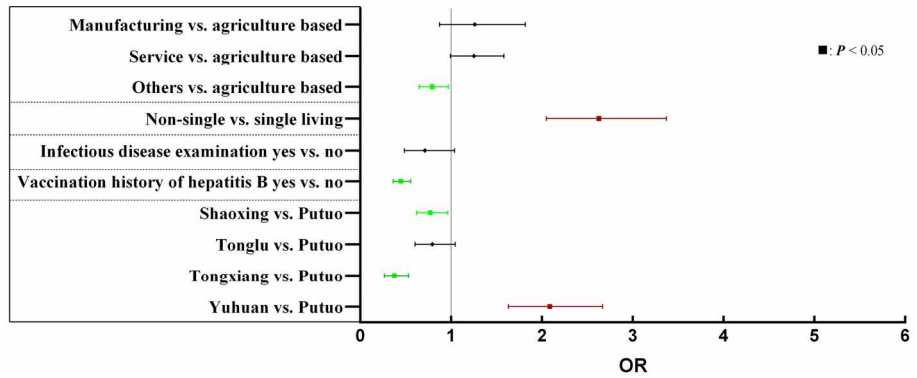


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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	3
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	18
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6,9
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	6
		(b) Describe any methods used to examine subgroups and interactions	
		(c) Explain how missing data were addressed	
		(d) If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest	7,8,9 7
Outcome data	15*	Report numbers of outcome events or summary measures	7
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	9-12
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	13-15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	16
Generalisability	21	Discuss the generalisability (external validity) of the study results	16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

The prevalence and influencing factors of hepatitis B among a rural residential population in Zhejiang Province, China: a cross-sectional study

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1 Title: The prevalence and influencing factors of hepatitis B among a rural residential population in
2 Zhejiang Province, China: a cross-sectional study

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34 **ABSTRACT**

35 **Objectives** To reveal the prevalence and associated influencing factors of hepatitis B among a
36 rural residential population in Zhejiang, China, so as to help develop specific control strategies.

37 **Methods** We conducted a cross-sectional study among a rural residential population in Zhejiang,
38 China. Stratified multistage cluster sampling was utilized in five districts, a structured
39 questionnaire was used to collect the information such as age, gender, education, occupation,
40 living status, and other health related information of the participants by the trained local staff,
41 participants' HBV infection status were determined by chemiluminescence immunoassay test.
42 Univariate and multivariate analyses were applied to evaluate the influencing factors of HBV
43 infection. The odds ratio of each related factor was assessed with or without adjustment separately.

44 **Results** The mean age of the 16601 participants, including 7881 males and 8720 females, who
45 completed the survey was 40.28 ± 19.47 years. The positive rate of hepatitis B surface antigen
46 (HBsAg) was 4.04% (95% CI: 3.74%-4.35%), and 3.85% after standardized by age and gender.
47 Univariate analysis showed that age, educational level, occupation, living status, history of taking
48 hepatitis B examinations, history of blood transfusion, vaccination, family history, coastal living,
49 and district were the potential influencing factors. Multivariate logistic regression indicated that
50 occupation, living status, history of taking hepatitis B examinations, vaccination and district were
51 the influencing factors. Undertaking a service-based tertiary industry job ($OR_a=1.19$, 95% CI:
52 0.94-1.51) and non-single living ($OR_a=2.84$, 95% CI: 2.17-3.70) might be risk factors, while
53 vaccination ($OR_a=0.43$, 95% CI: 0.34-0.53) and history of takeing hepatitis B examinations
54 ($OR_a=0.71$, 95% CI: 0.48-1.03) were potential protective factors.

55 **Conclusions** The prevalence of hepatitis B is at an intermediate epidemic level in a rural

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4 56 residential population in Zhejiang, China. Raising vaccination coverage, especially in adults, is a
5
6 57 suitable strategy for the prevention and control of hepatitis B.
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8
9 58 **Keywords:** Hepatitis B; Influencing factors; Cross-sectional study
10

11 59 **ARTICLE SUMMARY**

12 13 14 60 **Strengths and limitations of this study**

15
16 61 This study focused on the prevalence of hepatitis B in a rural residential population.
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19 62 The study involved a large rural residential population and the logistic regression model provided
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21 63 a quantified result of the influencing factors of hepatitis B.
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24 64 The main limitation of the study was that there could exist recall bias due to its cross-sectional
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26 65 design.
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67 INTRODUCTION

68 Hepatitis B is a potentially life-threatening infection caused by hepatitis B virus (HBV), which
69 attacks the liver and could cause both acute and chronic disease. Two billion people have evidence
70 of past or present HBV infection, and, globally, an estimated 240 million people are chronically
71 infected with hepatitis B virus [1 2]. More than 686000 people die annually due to complications
72 of hepatitis B, including cirrhosis and hepatocellular carcinoma (HCC)[3]. Previously, studies
73 revealed that the incidence of HBV-related HCC in adults remains high, and a high serum HBV
74 DNA level increases the risks of cirrhosis and HCC[4 5].

75 Overall, nearly half of the global population lives in areas of high hepatitis B endemicity[6]. The
76 global prevalence of HBV infection is heterogeneous[2], and the prevalence of hepatitis B is
77 highest in sub-Saharan Africa and East Asia, where 5%~10% of the adult population is chronically
78 infected[1]. The most recent large, nationwide survey in China was conducted in 2006, which
79 showed that the weighted positive rate of hepatitis B surface antigen (HBsAg) was 7.2% among
80 those aged 1 to 59 years, and the rate among children aged <5 years was only 1.0%[7]. According
81 to the disease distribution maps[2], hepatitis B in China was at a higher intermediate level. Since
82 that time, several studies[8-14] have been conducted to investigate the prevalence of hepatitis B in
83 different areas among the general population in mainland China. The reported prevalence was
84 3.49% in Beijing (2007)[8], 4.38% in adults in Northeast China (2007)[9], 7.44% in Anhui
85 Province (2006)[10], 5.17% in Henan Province (2006-2009)[11], 7.2% in Northwest China
86 (2010)[12], 3.17% in Sichuan blood donors (2010-2011)[13] and 2.73% in Beijing
87 (2013-2014)[14]. The rates were varied in different areas and at different time periods.

88 China has the largest rural population and labor resources around the world[15], and the rural

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4 89 population flow is the main component of China's population flow and has an important impact on
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6 90 the spatial pattern of the population in terms of regional economic and social development[16]. A
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9 91 hepatitis B prevalence of 3.7% (642) in a large sample was previously reported[17]; while another
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11 92 study[18] reported a 6% (124274) HBsAg positive rate among males in rural areas. The rural
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13 93 economy lags behind the urban economy in China, along with the resources of health and
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15 94 education.
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18 95 It is important to identify the prevalence of hepatitis B and the basic procedure for eradicating
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20 96 HBV infection. This study aimed to investigate the prevalence of hepatitis B and its potential
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22 97 influencing factors in a rural residential population in Zhejiang Province, China. By clearly
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24 98 indicating the characteristics of hepatitis B and its associated risk factors, we intend to develop
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26 99 specific prevention and control strategies.
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101 **METHODS**

102 **Study design**

103 A stratified multi-stage cluster sampling survey was conducted in five districts in Zhejiang
104 Province, China from January 2014 to December 2015. We took geographic characteristics and
105 economic levels into consideration when choosing the five districts in our study, coastal areas such
106 as Putuo and Yuhuan, inland areas such as Shaoxing, Tonglu, and Tongxiang, higher economic
107 level areas such as Shaoxing and Tongxiang, and lower economic level areas such as Putuo,
108 Yuhuan and Tonglu. Further stratified sampling was based on the population in rural town and
109 villages. All participants were registered as rural residents, who continuously resided in local for at
110 least six months. A total of 22000 people were recruited, and after 5539 people excluded with

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4 111 missing information, 16601 eligible participants were ultimately received completed survey. The
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6 112 research Ethics Committee at the First Affiliated Hospital, School of Medicine, Zhejiang
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9 113 University approved the study, and all participants gave the written informed consent.

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11 114 During the two-year of investigation, a structured questionnaire was designed to collect basic
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13 115 information such as age, gender, ethnicity, education, occupation, living status, medical insurance
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15 116 etc., and the potential factors related to HBV infection such as history of blood transfusion,
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17 117 surgery, vaccination of hepatitis B, family history of hepatitis B, and whether moving away from
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19 118 resident location more than three months etc.

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21 119 The investigation was completed by trained staff and local doctors. To increase the response rate,
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23 120 investigators were recommended to visit target houses at an appropriate time, such as nightfall.

24
25 121 One percent questionnaires were randomly selected to be checked for the completeness and
26
27 122 accuracy. During the investigation, blood samples (5 ml for individuals aged ≥ 6 years and 2 ml
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29 123 for children aged ≤ 5 years) were collected from the participants. Sera was separated and stored
30
31 124 at -20°C by laboratory staff from the local hospitals. After timely transported to our state key
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33 125 laboratory of the First Affiliated Hospital, College of Medicine, Zhejiang University, the serum
34
35 126 samples were tested by chemiluminescence immunoassay (CLIA) with Abbott reagents (Abbott
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37 127 Laboratories, Abbott Park, IL, USA). The positive rate of HBsAg in the population was
38
39 128 considered as the prevalence level of hepatitis B.

40 41 42 43 44 45 46 47 48 49 **Statistical analysis**

50
51 130 All collected data were doubly entered into an EpiData 3.1 software database by two staff,
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53 131 independently. Then, we checked the accuracy, consistency and logicity of the data. SAS 9.4
54
55 132 (SAS Institute Inc., Cary, NC, USA) software was used for data processing and analysis. Social
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4 133 demographic information was analysed by descriptive statistics. Univariate logistic analysis was
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6 134 used to identify potential influencing factors associated with hepatitis B infection; we selected the
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9 135 factors with $P < 0.1$ in the univariate model and conducted a stepwise multivariate logistic model
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11 136 to seek the independent risk factors for hepatitis B. Odds ratio (OR), 95% confidence interval
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13 137 (95% CI) and adjusted OR for each factor were also calculated. The statistical hypothesis test level
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15 138 was 0.05. GraphPad Prism 6.0 (GraphPad Software, Inc., La Jolla, CA, USA) was used to draw
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19 139 the figures.

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24 141 **RESULTS**25
26 142 **Characteristics of participants**

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29 143 Of the 22000 eligible participants, 16601 completed the survey with a response rate of 75.5%,
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31 144 including 7881 (47.47%) males and 8720 (52.53%) females in five districts. The mean age of the
32
33 145 participants was 40.28 ± 19.47 years. The prevalence of hepatitis B in all participants was 4.04%
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35 146 (95% CI: 3.74%-4.35%), and it was 3.85% standardized by age and gender when using the
36
37 147 population of Zhejiang Province as the standard population. The results showed that Zhejiang was
38
39 148 an intermediate epidemic area of hepatitis B.

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44 149 The distribution of the population and the prevalence between the different age groups are shown
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46 150 in Figure 1. We observed that the age below 20 years was the group that had the lowest prevalence
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49 151 of hepatitis B, while groups aged 41-60 years had the highest rates. There was a rapid increase in
50
51 152 the prevalence between those aged 21-25 years and 26-30 years.

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54 153 Among the five districts, Shaoxing had the most participants with a number of 5416 (32.65%),
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56 154 while Yuhuan had the smallest number with 1447 (8.72%) participants. The number of
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155 participants was 4370 (26.32%), 3523 (21.22%) and 1845 (11.11%) in the rest Putuo, Tonglu
 156 and Tongxiang areas, respectively. In our study, the prevalence of hepatitis B was highest in
 157 Yuhuan (9.81%), and lowest in Tongxiang (2.49%) (Figure 2).

158 We collected all the relevant data of the participants; participants' basic characteristics are listed in
 159 Table 1. Most of the participants' educational level was primary school or lower (44.25%), college
 160 level or higher was only 6.55%, and the group, which had the lowest prevalence (2.21%). Only
 161 13.48% of the participants had undergone hepatitis B examinations before, and few had a
 162 history of surgery (3.46%) or blood transfusion (0.57%). There were 6358 (38.30%)
 163 participants, who had a vaccination history of hepatitis B, and this figure was 75.5% in aged
 164 <20 years, and only 29.8% in aged >20 years. Of all participants, 5817 (35.04%) were living
 165 in coastal areas.

166
 167 Table 1 Characteristics of participants in the study and univariate analysis results

Variables/Values	Sample		HBsAg	
	size	Percent	positive	Prevalence
	(n)	(%)	(n)	(%)
Age**	16601	-	670	4.04
Gender				
Male	7881	47.47	324	4.11
Female	8720	52.53	346	3.97
Educational level**				
Primary school or lower	7346	44.25	305	4.15

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4	Junior school	5431	32.71	265	4.88
5					
6	High or polytechnic school	2736	16.48	76	2.78
7					
8					
9	College or higher	1088	6.55	24	2.21
10					
11	Occupation**				
12					
13					
14	Agriculture-based primary industry	5862	35.31	256	4.37
15					
16	Manufacturing-based secondary				
17		623	3.75	39	6.26
18	industry				
19					
20					
21	Service-based tertiary industry	2423	14.60	132	5.45
22					
23					
24	Other (Students or retired)	7693	46.34	243	3.16
25					
26	Living status**				
27					
28					
29	Single living	5299	31.92	81	1.53
30					
31	Non-single living	11302	68.08	589	5.21
32					
33					
34	Medical insurance				
35					
36	Out-of-pocket	339	2.04	13	3.83
37					
38					
39	Has medical insurance	16262	97.96	657	4.04
40					
41	History of taking hepatitis B examinations*				
42					
43					
44	Yes	2238	13.48	71	3.17
45					
46	No	14363	86.52	599	4.17
47					
48					
49	History of surgery**				
50					
51	Yes	575	3.46	48	8.35
52					
53	No	16026	96.54	622	3.88
54					
55					
56	History of blood transfusion				
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Yes	94	0.57	4	4.26
No	16507	99.43	666	4.03
Vaccination history of hepatitis B**				
Yes	6358	38.30	122	1.92
No	10243	61.70	548	5.35
History for being away 3 months				
Yes	843	5.08	39	4.63
No	15758	94.92	631	4.00
Family history of hepatitis B**				
Yes	446	2.69	69	15.47
No	16155	97.31	601	3.72
Living in coastal area**				
Yes	5817	35.04	296	5.09
No	10784	64.96	374	3.47
District**				
Putuo	4370	26.32	154	3.52
Shaoxing	5416	32.62	197	3.64
Tonglu	3523	21.22	131	3.72
Tongxiang	1845	11.11	46	2.49
Yuhuan	1447	8.72	142	9.81

168 *: P < 0.05; **: P < 0.0001.

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4 170 **Univariate and multivariate analysis**
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6 171 Univariate analysis showed that age, educational level, occupation, living status, history of taking
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8 172 hepatitis B examinations, vaccination history of hepatitis B, history of surgery, history for
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10 173 being away 3 months, family history of hepatitis B, and living in a coastal area and district
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12 174 could be the potential influencing factors associated with hepatitis B among the population
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14 175 (Table 1).
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18 176 The stepwise multivariate analysis showed that occupation, living status, history of taking
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20 177 hepatitis B examinations, vaccination history of hepatitis B and district were the independent
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22 178 influencing factors of hepatitis B in a rural residential population in Zhejiang. The age and
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24 179 gender adjusted model revealed that undertaking a service-based tertiary industry job
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26 180 ($OR_a=1.19$, 95% CI: 0.94-1.51), non-single living ($OR_a=2.84$, 95% CI: 2.17-3.70) were the
27
28 181 risk factors for hepatitis B prevalence; while having taken an examination of hepatitis B
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30 182 ($OR_a=0.71$, 95% CI: 0.48-1.03) and hepatitis B vaccinated ($OR_a=0.43$, 95% CI: 0.34-0.53)
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32 183 might be the protective factors for hepatitis B (Table 2). Figure 3 illustrates the values of OR
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34 184 and OR_a in the two logistic models.
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44 186 Table 2 Results of multivariate analysis for hepatitis B

Variables/Values	OR (95% CI)	<i>P</i> value	OR_a (95% CI)	<i>P</i> value
Occupation				
Agriculture-based primary industry	ref.		ref.	
Manufacturing-based	1.26(0.87-1.82)	0.2155	1.18(0.82-1.72)	0.3857

secondary industry				
Service-based tertiary industry	1.25(1.00-1.58)	0.0548	1.19(0.94-1.51)	0.1586
Other	0.79 (0.65-0.97)	0.0237	0.77(0.63-0.94)	0.0113
Living status				
Single living	ref.		ref.	
Non-single living	2.63(2.05-3.37)	<0.0001	2.84(2.17-3.70)	<0.0001
History of taking hepatitis B examinations				
Yes	0.72(0.49-1.04)	0.0787	0.71(0.48-1.03)	0.0705
No	ref.		ref.	
Vaccination history of hepatitis B				
Yes	0.45(0.36-0.56)	<0.0001	0.43(0.34-0.53)	<0.0001
No	ref.		ref.	
District				
Putuo	ref.		ref.	
Shaoxing	0.77(0.62-0.97)	0.0236	0.77(0.62-0.96)	0.0208
Tonglu	0.79(0.60-1.05)	0.1031	0.79(0.60-1.05)	0.1025
Tongxiang	0.38(0.27-0.53)	<0.0001	0.38(0.27-0.54)	<0.0001
Yuhuan	2.09(1.63-2.67)	<0.0001	2.09(1.63-2.67)	<0.0001

187 OR: odds ratio; OR_a: odds ratio adjusted by age and gender; ref.: reference.

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189 **DISCUSSION**

190 Prevalence of hepatitis B

191 Viral hepatitis is a leading cause of death and disability worldwide, deaths from acute infection,
192 cirrhosis and liver cancer were the tenth leading cause of death worldwide in 1990, while it ranked
193 seventh in 2013. The number of deaths worldwide attributable to viral hepatitis increased by 63%
194 from 1990 to 2013[19].

195 The prevalence of hepatitis B in all rural residential participants was 4.04% in Zhejiang (It was
196 3.85% standardized by age and gender). Our results indicated that the Zhejiang rural residential
197 population would be categorized as an intermediate group and that the hepatitis B prevalence was
198 significantly lower than reported 9.8% in 1992 and 7.2% in 2006 across China[7]. Following a
199 series of interventions conducted by the Chinese government, there was a significantly decline of
200 the hepatitis B epidemic. A larger nation-wide survey would be needed to assess the current
201 epidemic of hepatitis B in China to provide the epidemiological features and update the
202 controlling or prevention strategies, especially in the rural population.

203 Influencing factors of hepatitis B

204 There was no significant association between hepatitis B prevalence and age in our study.
205 Although, previous studies referred to age as a factor[20-22], and showed that an older age group
206 had a higher prevalence in the population. Our univariate analysis also indicated this phenomenon.
207 We thought this outcome was a result of confounding, by hepatitis B vaccination or other factors.
208 A former study also reported an inverse result[23]. For the factor of gender, the results were varied.
209 Previous studies[11 21 23-25] showed that the prevalence was higher in males than in females;
210 while there was no association found between gender and hepatitis B by one study[20], which was
211 similar to ours.

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4 212 Our study showed that education was not an independent influencing factor on hepatitis B, which
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6 213 was also noted in other studies[26 27]. However, there could be a possible trend of decreasing
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9 214 hepatitis B prevalence with increasing educational level from our univariate analysis in Table 1; it
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11 215 can be observed that the population with higher educational level had a lower hepatitis B
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13 216 prevalence. Potential reasonable explanations for these phenomena: among those higher-educated
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15 217 population, there are better prevention awareness of infectious diseases and a higher acceptance of
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17 218 vaccination; furthermore, having at least a college education (OR=2.55, 95% CI: 1.28-5.07) was
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19 219 an important predictor of vaccine completion[28].
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24 220 We found that only 13.48% of all participants had taken a hepatitis B examinations before, and
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26 221 there was a lower prevalence of hepatitis B among those participants; while in those participants
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28 222 who had not been previously examined, there was a higher prevalence. We could infer that those
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30 223 infected by hepatitis B virus, who had not been diagnosed by the examinations, could be the
31
32 224 potential sources of hepatitis B. By encouraging people to take part in hepatitis B examinations,
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34 225 along with routine physical examinations, we could benefit: First, find out those who are infected;
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36 226 Second, treat those infected ones immediately; Third, take the right opportunity to raise the
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38 227 awareness of hepatitis B among the population, especially in rural areas.
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44 228 Compared to other occupation types, service-based tertiary industry of occupation seemed to be a
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46 229 risk factor, along with non-single living (OR_a=2.84, 95% CI: 2.17-3.70). The factors mentioned
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48 230 above had the same feature: likely to result in more communications between people. We should
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50 231 take these into consideration, since hepatitis B is an infectious disease and has a sign of clustering
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52 232 among the population.
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56 233 Hepatitis B epidemics are scattered in different areas globally[2 22], and hepatitis B prevalences
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4 234 also varied among different districts in our study. These circumstances would be caused by
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6 235 geography, economic level, population density, living habits or other factors. Economic level
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9 236 seems to be a potential factor, since lower economic level areas such as Yuhuan had a higher
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11 237 prevalence and higher economic level areas such as Shaoxing and Tongxiang had a lower
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13 238 prevalence. Regardless of all features, we should consider district as a non-negligible factor,
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15 239 especially the district with a high prevalence, when developing and implementing strategies for
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18 240 fighting hepatitis B.

21 241 **Control strategies for hepatitis B**

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24 242 World Health Organization (WHO) adopted the first-ever global hepatitis strategy with a goal to
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26 243 eliminate viral hepatitis B and C as public health threats by 2030, which was defined as a
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28 244 reduction in incidence by 90% in new chronic infections and mortality by 65% for viral hepatitis
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31 245 B and C[29]. Currently, hepatitis B is a major health problem and has a significant socio-economic
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33 246 impact all over the world[30]. HBV vaccination is the mainstay of HBV prevention and is the
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35 247 most effective prevention strategy[31 32].

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39 248 The Chinese government has made great progresses with hepatitis B vaccination[33]: the national
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41 249 hepatitis B immunization plan was established in 1992. In 2002, the Global Alliance on Vaccine
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43 250 and Immunization (GAVI) partnered with the government of China to provide free hepatitis B
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45 251 vaccine[34] and fully integration into the routine immunization program, and the vaccine was
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48 252 provided completely free to infants, nationally in 2005[35]. The carrier rate in Chinese children
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50 253 aged <5 years fell to less than 1% in 2006, and to 0.32% in 2014, which was 10% in the 1990s[36].
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53 254 Recently, WHO estimated that new-borns in China, who received a timely birth dose (TBD) and
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56 255 third dose of hepatitis B vaccine (HepB3), was 96% and 99% respectively[37]. Our study showed
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4 256 that Hepatitis B vaccination ($OR_a=0.43$, 95% CI: 0.34-0.53) was the protective factors for hepatitis
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6 257 B, and the same results have been observed[12 13 26].
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9 258 Regarding vaccination coverage related to the economy status, a former study suggested that
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11 259 higher HBV vaccination coverage rates among adults were obtainable. The user fees, time needed
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13 260 for vaccination and travel costs acted as economic barriers to vaccination[38]. Hepatitis B
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15 261 vaccination has been reported as low as 13.89% in rural China[39]. We call for strengthening
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17 262 HBV vaccination in rural areas, and raising the vaccine coverage rate.
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21 263 Our survey also showed that the vaccination rate was 75.5% in aged <20 years, while it was only
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23 264 29.8% in aged >20 years. There was a trend that the rate of hepatitis B vaccination was increased
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25 265 when the vaccination programme conducted and expanded since 1992, along with decreasing of
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27 266 the nationwide hepatitis B prevalence. Preventing hepatitis B through vaccination is currently the
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29 267 most efficient way to decrease HBV-related cirrhosis and liver cancer incidence, and reduce the
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31 268 HBV reservoir[30]. The role of the vaccination programme for the effective control of hepatitis B
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33 269 should be emphasized[40]. In the near future, we should focus hepatitis B vaccination efforts on
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35 270 adults, under the consideration of policies for universal vaccination, especially in those areas with
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37 271 high hepatitis B endemicity.
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45 46 273 **LIMITATION**

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49 274 This study was cross-sectionally designed, and we could not exclude the acute infection case; thus
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51 275 the hepatitis B prevalence may be overestimated in the population when using the HBsAg positive
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53 276 rate as the level of chronic HBV infection, and there was also a certainty of recall bias in this
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55 277 study design. Additionally, the sample sizes were not balanced between districts in our study. We
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4 278 considered taking a vaccination history of hepatitis B as an indicator of vaccine success due to the
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6 279 effectiveness of vaccination[30]. To interpret the results, we simply divided the variables into a
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9 280 few groups, such as occupation. A more precise classification of factors could be assessed in later
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11 281 studies, along with more potential factors, such as family income.
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15 16 283 **CONCLUSIONS**

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18 284 In conclusion, though our study showed that the Zhejiang rural area is categorized as an
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21 285 intermediate epidemic level for hepatitis B in China, there remains the important issue and
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23 286 formidable challenge of dealing with the problem of hepatitis B in rural areas among the resident
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25 287 population. Specific methods such as raising the coverage of vaccination particularly in adults, are
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27 288 suitable and effective strategies to prevent and control hepatitis B in Zhejiang rural areas.
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29 289 Furthermore, increasing the percentage of the hepatitis B examinations may also be considered as
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31 290 a potential strategy. The significant findings in this study, with potential implications for public
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33 291 health, would be helpful to China and other countries for the fight against hepatitis B.
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43 294 The funders had no role in study design, data collection, data analysis or writing of the report. The
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45 295 corresponding author had full access to all the data in the study and had the final responsibility for
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47 296 the decision to submit for publication.
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51 297 **Footnotes**

52
53 298 SY and CD contributed equally.
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56 299 **Contributors**

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4 300 LL, JR, BR, JY and SY conceived and designed the study. CD, YC, JW, CY, CP, KX, MD, YL, JL,
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6 301 PY, WR, YQ, QC and YZ collected data, cleaned, and analysed the data and revised the paper. CD
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9 302 and SY wrote the first draft of the paper, contributed to figures and paper preparation and all
10
11 303 authors critically revised the paper and gave final approval for publication.
12

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17
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26
27 310 Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital,
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29 311 College of Medicine, Zhejiang University, China] [2016KF11].
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32 33 34 312 **Competing interests**

35
36 313 None declared.
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38 39 314 **Data sharing statement**

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41 315 No additional data are available.
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4 424 Figure Legends:
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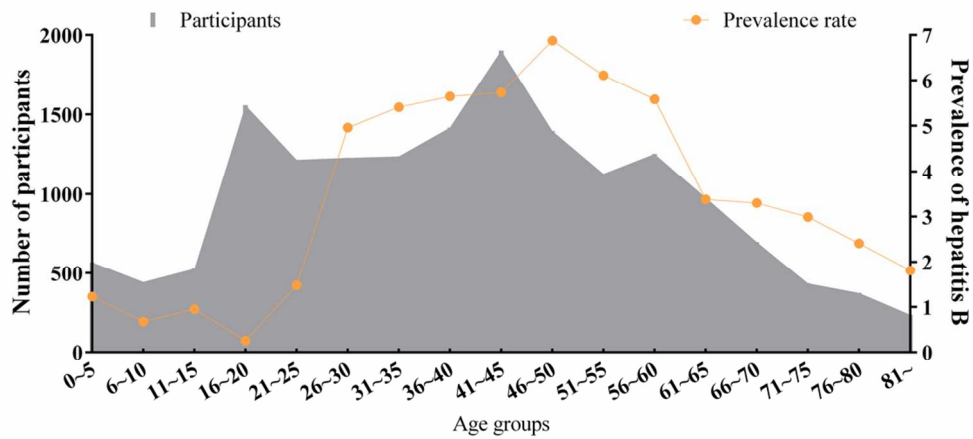
6 425 Figure 1 The prevalence of hepatitis B among different age groups
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8 426 Figure 2 The distribution of participants and prevalence of hepatitis B in different districts
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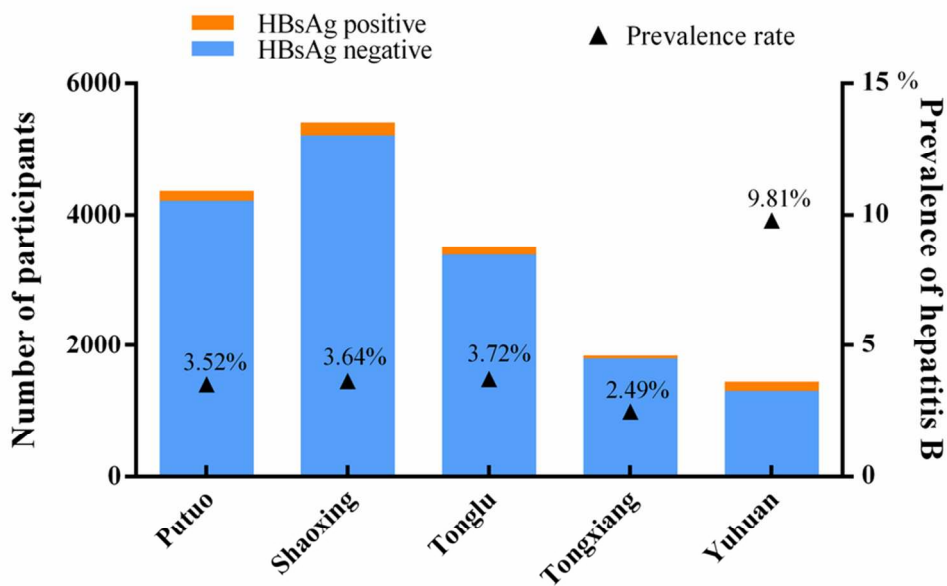
10 427 Figure 3 The values of OR and OR_a in the logistic models.
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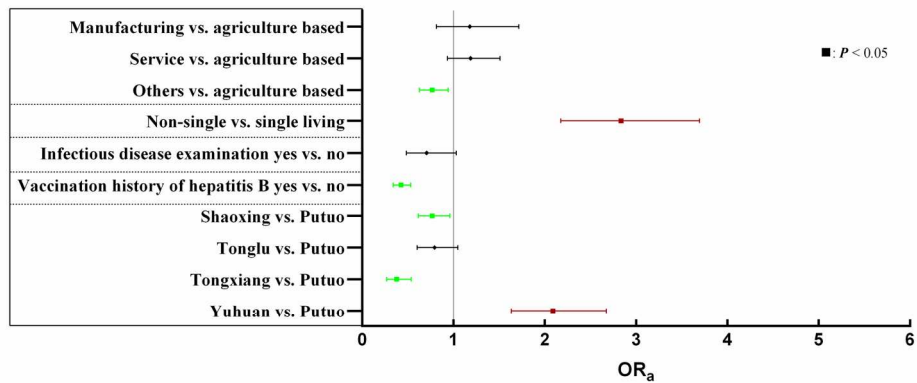
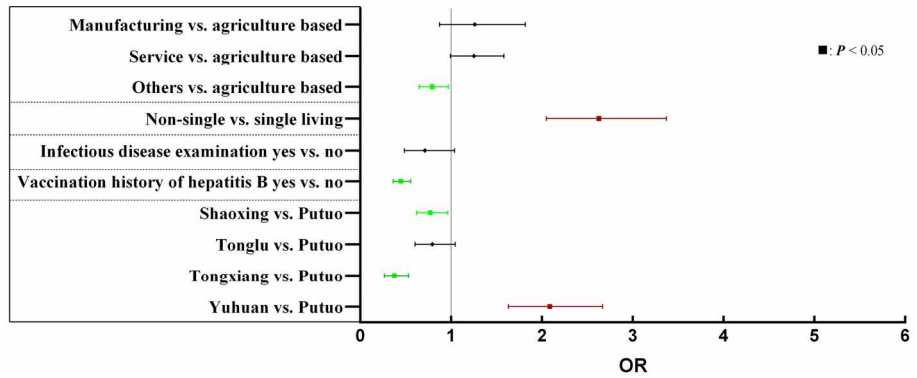


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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1, 3
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4, 5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6, 7
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7
		(b) Describe any methods used to examine subgroups and interactions	-
		(c) Explain how missing data were addressed	6,7
		(d) If applicable, describe analytical methods taking account of sampling strategy	6,7
		(e) Describe any sensitivity analyses	-
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7, 8
		(b) Indicate number of participants with missing data for each variable of interest	7
Outcome data	15*	Report numbers of outcome events or summary measures	7
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-11
		(b) Report category boundaries when continuous variables were categorized	-
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	-
Discussion			
Key results	18	Summarise key results with reference to study objectives	13-16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	18
Generalisability	21	Discuss the generalisability (external validity) of the study results	18
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	18

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.