

# The economic burden of influenza-like illness among children, chronic disease patients and the elderly in China: a national cross-sectional survey

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## Research Article

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# Abstract

**Background:** The disease burden of seasonal influenza is substantial in China, while there is still a lack of nation-wide economic burden estimates. This study aims to examine influenza-like illness (ILI) prevalence, healthcare seeking behaviors, economic impact of ILI and its influencing factors among children, chronic disease patients and the elderly during the 2018–19 influenza season.

**Methods:** From August to October 2019, 6668 children’s caregivers, 1735 chronic disease patients, and 3849 elderly people were recruited from ten provinces in China to participate in an on-site survey. The economic burden of ILI consisted of direct (medical or non-medical) and indirect burden, and multivariate linear regression was adopted to predict the influencing factors of total economic burden.

**Results:** There were 45.73% children, 16.77% chronic disease patients and 12.70% elderly people reporting ILI, and most participants chose “Outpatient service only”, “Over-the-counter (OTC) medication only” or “Outpatient + OTC” after ILI. The average total economic burden of ILI was 1848 yuan (USD266.1) for children, 1105 yuan (USD159.1) for chronic disease patients and 2064 yuan (USD297.2) for the elderly. Multivariate linear regression showed that boys, the only child in family, and urban adult residents tended to have larger economic burden after ILI.

**Conclusions:** Large economic burden of ILI was highlighted, especially among the elderly with less income and larger medical burden, as well as children with higher prevalence and higher self-payment ratio. It is important to adopt targeted interventions for high-risk groups, and this study can help national-level decision-making on the introduction of influenza vaccination as public health project.

## 1. Background

Annual influenza epidemics result in substantial morbidity and mortality across the globe, with a large share of the total disease burden occurring in low- and middle-income countries (LMICs).<sup>[1]</sup> As estimated by the World Health Organization (WHO) in 2018, the annual epidemics of seasonal influenza could result in about 3 to 5 million severe cases and 290–650 thousand influenza-associated deaths.<sup>[2]</sup> The disease burden of seasonal influenza is also substantial in China. A recent study estimated the influenza-associated excess respiratory mortality in mainland China, and found that about 88 thousand influenza-associated excess respiratory deaths occurred annually, corresponding to 8.2% of respiratory deaths.<sup>[3]</sup>

As suggested in the WHO position paper, those at particular risk of developing severe disease, i.e. disease resulting in hospitalization or death, or those at increased risk of exposure to influenza virus, were identified as risk groups for influenza, including children aged <5 years, the elderly, pregnant women, individuals with underlying health conditions, and healthcare workers. Illness severity and mortality are the greatest in high-risk groups, and so are the associated health care costs and productivity losses. Accordingly, the Technical Guidance for Influenza Vaccination in China (2019–20) clearly pointed out that children (aged between 6 to 59 months), patients with chronic diseases, and the elderly (aged 60

years old or above) are among the priority groups for influenza vaccination, together with healthcare workers, family members and caregivers of infants under 6 months, and pregnant women.<sup>[4]</sup>

However, influenza vaccination has not been included in China's National Immunization Program (NIP), and the expenses are paid totally out of pocket on most occasions, even for the priority groups.<sup>[5]</sup> The coverage rate of influenza vaccination in China is extremely low in the past 15 years, with only 2% of the entire population being immunized, far lower than that of western developed countries and some developing countries in Asia and South America.<sup>[3]</sup> In this case, it is important to consider the economic burden of influenza disease at the national level to make informed and evidence-based decisions.

Currently, sufficient data to precisely estimate the economic burden of influenza, especially in developing countries, are not available. A systematic review in 2015 suggested that information on the economic burden of influenza in LMICs was scarce and incomplete.<sup>[6]</sup> In China, there were several studies examining the incidence and economic burden of influenza, but most of them were conducted at hospital or provincial level.<sup>[7-11]</sup> Given the lack of economic burden estimates of seasonal influenza across China, the present study aims to examine influenza-like illness (ILI) prevalence, influenza-related healthcare seeking behaviors, the economic impact of ILI and its influencing factors among children, chronic disease patients and the elderly during the 2018–19 influenza season in ten Chinese provinces.

## 2. Methods

### 2.1. Study population and sampling

In August to October 2019, a total of 148 community health centers from 10 provinces in China were approached to join the national survey on the economic burden of season influenza among three priority groups, including children aged 6–59 months, chronic disease patients aged 18–59 years, and the elderly aged above 60 years (Financing Strategies of Influenza Vaccination in China, NCT04038333).<sup>[12]</sup> For children aged 6–59 months, we asked their parents or grandparents who accompanied them to health centers to finish the compulsory immunization procedure.<sup>[4]</sup> For chronic disease patients and the elderly, we asked them in health centers or gathered them in neighborhood committees. This study was ethically reviewed and approved by the Peking University Institutional Review Board (IRB00001052-19076), and written informed consent was obtained from individual or guardian participants.

We calculated the sample size under the assumption that the predicted prevalence of ILI would be 40% among children, 10% among the elderly, and 20% among those with chronic diseases. With an allowable error of 5%, a sample size of 369, 138, and 246 was determined for the three groups in each province. To allow for disqualification of incomplete questionnaires, we increased the sample size by 10%, with a final target sample population of 4059, 1518, and 2706. In practice, we collected a larger sample size than expected to increase the reliability of the results.

The survey adopted a multistage sampling method. First, ten provinces/municipalities were selected based on the Division of Central and Local Financial Governance and Expenditure Responsibilities in the Healthcare Sector released by the State Council in 2018, which stratifies the 31 provinces/municipalities in mainland China into five layers.<sup>[13]</sup> The division of expenditure responsibility between central and local governments differed across layers, with ratios of 8:2 (first layer), 6:4, 5:5, 3:7, and 1:9 (fifth layer). In terms of location, socioeconomic development, and accessibility, ten provinces/municipalities (3, 3, 1, 1, and 2 in each layer) were chosen, with their location and 2018 per capita GDP rank (e.g., 1/31), as shown in Fig. 1. Second, in each province/municipality, a capital city or well-developed district (in municipalities) and a non-capital city or less-developed district were selected. Third, two subdistricts/counties were chosen in each city or district, in which three or more immunization centers (in community health centers or township clinics) and the corresponding neighborhood committees were approached to participate in the survey.

## 2.2. Measures

The on-site survey was conducted by trained interviewers using a specially-designed online PAD questionnaire system. Automatic logical proofreading was adopted in the online questionnaire to reduce input errors and missing values. In addition, interview recordings are uploaded and spot-checked by quality control personnel to find and correct problems in time. The structured online questionnaire can be divided into four parts: (1) socio-demographics such as age, gender, education level, household monthly per capita income, place of residence (urban or rural), self-reported health status, etc.; (2) whether had ILI in the past season; (3) health care seeking behaviors after ILI, including outpatient service, inpatient service, and over-the-counter (OTC) medication; (4) economic burden of the latest ILI in terms of direct (medical and non-medical) costs and indirect costs.

The economic burden of diseases consists of direct (medical or non-medical), indirect and intangible burdens. The direct medical burden refers to the costs medical services, and direct non-medical burden refers to the costs of supporting activities in the treatment process, including transportation, accommodation, nutrition, etc. The indirect economic burden is the loss of effective labor force caused by the disease. The intangible burden refers to the pain, anxiety, inconvenience, and subsequent decline in the quality of life to patients and their families. In view of the difficulty to measure intangible burden, studies on economic burden of diseases usually focus on direct and indirect burdens.<sup>[14]</sup>

According to the WHO standard ILI case definition, body temperature  $\geq 38$  °C with either cough or sore throat was used in the present study to distinguish influenza from other respiratory illnesses.<sup>[15]</sup> In the present study, for each interviewee (or their child aged 6–59 months) who reported ILI in the past season, their health care seeking behaviors and economic costs after the ILI were further examined. Direct medical costs were asked in terms of services types (outpatient services, hospitalization services, and/or OTC medication) and co-payment in each service type (self-paid expenses and medical insurance reimbursement). Direct non-medical costs were inquired from aspects of transportation, nutrition/food, accommodation, and nursing worker hiring. Indirect burden was obtained by asking the lost labor days of

the respondents and their families, and calculating the economic cost based on the per capita GDP of each province in 2018.<sup>[16]</sup>

### **2.3. Statistical analysis**

We produced summary statistics using frequencies and proportions for categorical variables, and means and standard deviations for continuous variables. The chi-square and Mann-Whitney tests were used to assess differences in sample characteristics. The economic burden values of ILI was displayed as means and 95% confidence intervals (CI). Multivariate linear regression analysis was adopted to predict the influencing factors (including age, gender, household income, place of residence, etc.) of total economic burden (in log form), and results were shown as coefficients and 95% CIs. A two-sided p-value below 0.05 was considered statistically significant. The reported direct medical and non-medical costs were adjusted for provincial health care price index and consumer price index, respectively, according to the China Statistical Yearbook 2019.<sup>[16]</sup> All data were analyzed using Stata version 14.0 (Stata Corp., College Station, TX, USA).

## **3. Results**

### **3.1. Study Sample Characteristics**

A total of 12252 valid questionnaires (6668 for children, 1735 for patients with chronic diseases, and 3849 for the elderly) were received, with an effective response rate of 99.80%. Table 1 shows the general characteristics of participants in the analysis of influenza-like illness economic burden. Overall speaking, 45.73% of children, 16.77% of chronic disease patients and 12.70% of elderly people reported to have ILI in the past season. Among the children, there were slightly more boys than girls (3497 vs. 3171), and the caregivers of 5812 out of 6668 children reported good health status for their children. In the other two groups, patients with chronic diseases 50–59 years of age accounted for 77.8%, and the elderly 60–79 years of age accounted for 91.9%. More women participated in the survey in both groups, and the majority of them had fair or poor self-reported health status. We further compared the distribution of age and gender in the three groups with that in China Population and Employment Statistics Yearbook 2019<sup>[17]</sup> and found similar results, indicating the national representativeness of the population collected in this study.

Table 1  
 Characteristics of 12252 participants included in the analysis.

	Children aged 6–59 months			Chronic disease patients aged 18–59 years			Elderly aged above 60 years		
	n	ILI cases, n (%)	<i>p</i> -value	n	ILI cases, n (%)	<i>p</i> -value	n	ILI cases, n (%)	<i>p</i> -value
Total	6668	3049 (45.73)		1735	291 (16.77)		3849	489 (12.70)	
Age (years)			< 0.01			< 0.01			0.40
< 1	1768	492 (27.83)		–	–		–	–	
1	1959	976 (49.82)		–	–		–	–	
2	1241	645 (51.97)		–	–		–	–	
3–5	1700	936 (55.06)		–	–		–	–	
18–39	–	–		72	24 (33.33)		–	–	
40–49	–	–		313	58 (18.53)		–	–	
50–59	–	–		1350	209 (15.48)		–	–	
60–69	–	–		–	–		2045	273 (13.35)	
70–79	–	–		–	–		1491	181 (12.14)	
≥ 80	–	–		–	–		313	35 (11.18)	
Gender			0.06			0.69			0.12
Female	3171	1412 (44.53)		1139	194 (17.03)		2334	281 (12.04)	
Male	3497	1637 (46.81)		596	97 (16.28)		1515	208 (13.73)	
The only child in the family			< 0.01			–			–

	Children aged 6–59 months		Chronic disease patients aged 18–59 years		Elderly aged above 60 years		
Yes	3038	1320 (43.45)	–	–	–	–	
No	3630	1729 (47.63)	–	–	–	–	
Household monthly per capita income (thousand yuan) <sup>a</sup>			<i>0.62</i>		<i>0.24</i>		< 0.05
Mean (SD)	2.66 (2.76)	2.68 (2.69)	1.84 (2.41)	1.99 (2.31)	1.70 (1.61)	1.56 (1.86)	
Place of residence			<i>0.33</i>		<i>0.94</i>		< 0.01
Rural	2814	1267 (45.02)	831	140 (16.85)	1742	255 (14.64)	
Urban	3854	1782 (46.24)	904	151 (16.7)	2107	234 (11.11)	
Basic medical insurance type <sup>b</sup>			<i>0.15</i>		<i>0.20</i>		< 0.01
Medical insurance for urban and rural residents	4081	1842 (45.14)	1212	193 (15.92)	2551	356 (13.96)	
Urban employee medical insurance	2380	1121 (47.10)	492	90 (18.29)	1189	118 (9.92)	
Without basic medical insurance	207	86 (41.55)	31	8 (25.81)	109	15 (13.76)	
Self-reported health status			< 0.01		< 0.01		< 0.01
Good	5812	2536 (43.63)	596	74 (12.42)	1578	141 (8.94)	
Fair or poor	856	513 (59.93)	1139	217 (19.05)	2271	348 (15.32)	
Province			< 0.01		< 0.05		< 0.01



	Children aged 6–59 months		Chronic disease patients aged 18–59 years		Elderly aged above 60 years	
Yunnan	629	264 (41.97)	155	28 (18.06)	308	60 (19.48)
Gansu	742	270 (36.39)	225	48 (21.33)	577	118 (20.45)
Chongqing	848	259 (30.54)	222	23 (10.36)	576	38 (6.60)
Jilin	681	342 (50.22)	170	25 (14.71)	391	29 (7.42)
Henan	630	328 (52.06)	162	36 (22.22)	314	66 (21.02)
Jiangxi	621	352 (56.68)	165	31 (18.79)	330	41 (12.42)
Shandong	626	314 (50.16)	172	20 (11.63)	355	36 (10.14)
Guangdong	621	347 (55.88)	153	31 (20.26)	334	42 (12.57)
Beijing	668	297 (44.46)	153	20 (13.07)	332	21 (6.33)
Shanghai	602	276 (45.85)	158	29 (18.35)	332	38 (11.45)
<sup>a</sup> 1 yuan = USD0.144 on 13th August 2020.						
<sup>b</sup> Basic medical insurance type in column refer to adult respondents.						

Among children aged 6–59 months, older children had higher possibility of catching ILI than younger children ( $p < 0.01$ ), and the only child in the family was less likely to have ILI than those living in families with more than one child ( $p < 0.01$ ). Among chronic disease patients aged 18–59 years, those with younger age were more likely to catch ILI than older adults ( $p < 0.01$ ). Among the elderly aged above 60 years, respondents with higher household monthly per capita income ( $p < 0.05$ ), living in urban areas ( $p < 0.01$ ), or having urban employee medical insurance ( $p < 0.01$ ) had lower possibility of having ILI. In the three groups, respondents with fair or poor self-reported health status had higher risk of catching ILI than those with good self-reported health status ( $p < 0.01$ ).

### 3.2. Health care seeking behaviors

Table 2 shows the distribution of health care seeking behaviors among 3829 participants after the latest ILI by calculating the number of ILI cases leading to outpatient visits, hospitalization, and OTC medication. As the table indicates, most participants chose “Outpatient service only”, “OTC medication

only” or “Outpatient + OTC” after ILI, accounting for 84.29% children, 84.53% chronic disease patients and 73.42% elderly people.

Table 2  
Health care seeking behaviors of 3829 participants after influenza-like illness.

	Children aged 6–59 months		Chronic disease patients aged 18–59 years		Elderly aged above 60 years	
	n	%	n	%	n	%
<b>Total</b>	3049	100	291	100	489	100
<b>Health care seeking behaviors</b>						
Outpatient service only	1162	38.11	100	34.36	159	32.52
Inpatient service only	46	1.51	4	1.37	26	5.32
OTC medication only <sup>a</sup>	316	10.36	69	23.71	123	25.15
Outpatient + Inpatient	172	5.64	10	3.44	40	8.18
Outpatient + OTC	1092	35.82	77	26.46	77	15.75
Inpatient + OTC	25	0.82	1	0.34	14	2.86
Outpatient + Inpatient + OTC	134	4.39	10	3.44	18	3.68
No treatment	102	3.35	20	6.87	32	6.54
<b>Service types</b>						
Outpatient service	2560	83.96	197	67.70	294	60.12
Inpatient service	377	12.36	25	8.59	98	20.04
OTC medication	1567	51.39	157	53.95	232	47.44
<sup>a</sup> OTC, over-the-counter.						

More specifically, when ILI occurred in children, 38.11% of them only seek outpatient service, 35.82% accepted a combination of outpatient treatment and OTC medication, and 10.36% only purchased OTC drugs outside the hospital. There were also 102 children (3.35%) not receiving any medical services after ILI. In terms of service type, 83.96% of children received outpatient service after ILI, 12.36% had inpatient service, and 51.39% received OTC medication. As for chronic disease patients, 34.36% of them only seek

outpatient service after ILI, 26.46% received outpatient treatment and OTC medication, and 23.71% only purchased OTC drugs. There were 20 chronic disease patients (6.87%) not receiving any medical services after ILI. In terms of service type, 67.70%, 8.59% and 53.95% of chronic disease patients received outpatient service, inpatient service and OTC medication, respectively. For the elderly after ILI, 32.52% of them only seek outpatient service, 25.15% only received OTC medication, and 15.75% accepted a combination of outpatient treatment and OTC medication. There were 32 elderly people (6.54%) not receiving any medical services after ILI. In terms of service type, 60.12%, 20.04% and 47.44% of elderly people received outpatient service, inpatient service and OTC medication, respectively.

### **3.3. Economic burden of influenza-like illness**

Table 3 shows the economic burden of children, chronic disease patients, and the elderly for the latest ILI during the 2018–19 influenza season, in which direct medical and non-medical costs were adjusted for provincial health care price index and consumer price index, respectively, and indirect cost was calculated based on the per capita GDP of each province. As the results indicate, the economic burden of ILI for a child was about 1848 yuan (1 yuan = USD0.144 on 13th August 2020), including reimbursed medical expenses of 272 yuan, self-paid medical expenses of 997 yuan, direct non-medical expenses of 212 yuan, and indirect cost of 366 yuan. The average economic burden for chronic disease patients was about 1105 yuan, including reimbursed medical expenses of 335 yuan, self-paid medical expenses of 386 yuan, direct non-medical expenses of 102 yuan, and indirect cost of 283 yuan. The elderly had much higher average economic burden of about 2064 yuan, including reimbursed medical expenses of 766 yuan, self-paid medical expenses of 778 yuan, direct non-medical expenses of 162 yuan, and indirect cost of 358 yuan. For children and chronic disease patients, outpatient and inpatient costs accounted for the vast majority of direct medical expenses, and nutrition/food and transportation accounted for most direct non-medical expenses. For the elderly, only inpatient cost accounted for the vast majority of direct medical expenses, and nutrition/food and accommodation accounted for most direct non-medical expenses.

Table 3  
The economic burden of influenza-like illness for 3829 participants.

	Children aged 6–59 months		Chronic disease patients aged 18–59 years		Elderly aged above 60 years	
	Mean	95% CI <sup>a</sup>	Mean	95% CI	Mean	95% CI
<b>Total direct medical cost (yuan)<sup>b,e</sup></b>	<b>1269</b>	<b>(1168, 1370)</b>	<b>721</b>	<b>(512, 930)</b>	<b>1544</b>	<b>(1200, 1888)</b>
Outpatient service	644	(595, 694)	239	(184, 293)	384	(281, 488)
Inpatient service	523	(454, 593)	394	(192, 595)	1053	(763, 1343)
OTC medication <sup>f</sup>	102	(93, 110)	89	(64, 113)	106	(75, 138)
<b>Reimbursed direct medical cost (yuan)<sup>b</sup></b>	<b>272</b>	<b>(234, 310)</b>	<b>335</b>	<b>(194, 477)</b>	<b>766</b>	<b>(568, 963)</b>
Outpatient service	88	(67, 108)	85	(54, 116)	153	(95, 210)
Inpatient service	179	(151, 206)	239	(102, 375)	605	(426, 784)
OTC medication	6	(4, 8)	11	(6, 17)	8	(5, 12)
<b>Self-paid direct medical cost (yuan)<sup>b</sup></b>	<b>997</b>	<b>(919, 1074)</b>	<b>386</b>	<b>(295, 477)</b>	<b>778</b>	<b>(595, 961)</b>
Outpatient service	556	(515, 597)	154	(114, 193)	232	(167, 296)
Inpatient service	345	(295, 395)	155	(75, 235)	448	(302, 595)
OTC medication	96	(88, 103)	77	(54, 101)	98	(67, 130)
<b>Direct non-medical cost (yuan)<sup>c</sup></b>	<b>212</b>	<b>(186, 238)</b>	<b>102</b>	<b>(31, 172)</b>	<b>162</b>	<b>(68, 256)</b>
Transportation	79	(70, 87)	50	(-8, 109)	21	(8, 34)
Nutrition/food	107	(93, 121)	34	(18, 49)	96	(12, 180)
Accommodation	19	(12, 27)	18	(-2, 38)	40	(3, 76)
Nursing worker hiring	8	(-5, 21)	0	(0, 0)	5	(-2, 12)
<b>Indirect cost<sup>d</sup></b>	<b>366</b>	<b>(341, 391)</b>	<b>283</b>	<b>(199, 366)</b>	<b>358</b>	<b>(265, 452)</b>

	Children aged 6–59 months		Chronic disease patients aged 18–59 years		Elderly aged above 60 years	
Lost labor days of respondents' families	2	(1.9, 2.1)	0.7	(0.4, 1)	2	(1.5, 2.6)
Lost labor days of the respondents	–	–	1.1	(0.8, 1.5)	0.9	(0.5, 1.3)
<b>Total economic costs</b>	<b>1848</b>	<b>(1720, 1976)</b>	<b>1105</b>	<b>(830, 1380)</b>	<b>2064</b>	<b>(1650, 2478)</b>

<sup>a</sup> CI, confidence interval.

<sup>b</sup> Direct medical cost was adjusted for provincial health care price index in China Statistical Yearbook 2019.

<sup>c</sup> Direct non-medical cost was adjusted for provincial consumer price index in China Statistical Yearbook 2019.

<sup>d</sup> Indirect cost was calculated based on the per capita GDP of each province in China Statistical Yearbook 2019.

<sup>e</sup> 1 yuan = USD0.144 on 13th August 2020.

<sup>f</sup> OTC, over-the-counter.

### 3.4. Influencing factors of total economic burden

Table 4 shows the results of multivariate linear regression to predict the influencing factors of total economic burden (in log form), including age, gender, whether the only child in the family (only for children), household income, place of residence, basic medical insurance type, and self-reported health status. As 91 children, 16 chronic disease patients and 32 elderly people reported zero total economic burden, we calculated the log form for these respondents as  $\log(\text{total cost} + 1)$ .

Table 4  
Linear regression of total economic burden (in log form) for the three groups.

Factors	Children		Chronic disease patients		Elderly	
	Coef.	95% CI <sup>a</sup>	Coef.	95% CI	Coef.	95% CI
Age (years)						
< 1	Ref.		-	-		-
1	0.09	(-0.10, 0.29)	-	-		-
2	-0.03	(-0.24, 0.18)	-	-		-
3-5	-0.03	(-0.22, 0.16)	-	-		-
18-39	-	-	Ref.			-
40-49	-	-	-0.93	(-1.93, 0.08)		-
50-59	-	-	-1.09*	(-2.01, -0.17)		-
60-69	-	-	-	-	Ref.	
70-79	-	-	-	-	0.13	(-0.33, 0.58)
≥ 80	-	-	-	-	0.02	(-0.84, 0.89)
Gender						
Female	Ref.		Ref.		Ref.	
Male	0.16*	(0.04, 0.29)	-0.13	(-0.64, 0.37)	-0.34	(-0.79, 0.11)
The only child in the family	0.28*	(0.15, 0.41)	-	-	-	-
Household monthly per capita income (thousand yuan) <sup>b</sup>	-0.02	(-0.04, 0.01)	0.03	(-0.09, 0.14)	0.00	(-0.15, 0.15)
Place of residence						
Rural	Ref.		Ref.		Ref.	
Urban	0.04	(-0.09, 0.18)	-0.62*	(-1.17, -0.08)	-0.77*	(-1.29, -0.25)

Factors	Children		Chronic disease patients		Elderly	
	Coef.	95% CI <sup>a</sup>	Coef.	95% CI	Coef.	95% CI
Basic medical insurance type <sup>c</sup>						
Medical insurance for urban and rural residents	Ref.		Ref.		Ref.	
Urban employee medical insurance	-0.01	(-0.15, 0.13)	0.28	(-0.34, 0.90)	0.47	(-0.13, 1.08)
Without basic medical insurance	0.11	(-0.27, 0.49)	-0.77	(-2.23, 0.69)	-0.48	(-1.74, 0.78)
Self-reported good health status	-0.53*	(-0.70, -0.35)	0.48	(-0.08, 1.04)	-0.68*	(-1.16, -0.21)
* Significant at the 5% level.						
<sup>a</sup> CI, confidence interval.						
<sup>b</sup> 1 yuan = USD0.144 on 13th August 2020.						
<sup>c</sup> Basic medical insurance type in column refer to adult respondents.						

Among children, the economic burden of boys (Coef. = 0.16, 95% CI 0.04–0.29,  $p < 0.05$ ) and the only child in the family (Coef. = 0.28, 95% CI 0.15–0.41,  $p < 0.05$ ) after ILI was larger than that of girls or those living in families with two or more children. In terms of self-reported health status, children reported to have good health status had smaller economic burden (Coef. = -0.53, 95% CI -0.70–-0.35,  $p < 0.05$ ) than those with fair or poor health status. Among chronic disease patients, those aged 50–59 years old suffered from lower economic burden after ILI (Coef. = -1.09, 95% CI -2.01–-0.17,  $p < 0.05$ ) compared with younger respondents who developed chronic diseases at earlier age. Besides, patients living in urban areas had smaller economic burden (Coef. = -0.62, 95% CI -1.17–-0.08,  $p < 0.05$ ) than those living in rural areas. Among the elderly, the economic burden of urban residents (Coef. = -0.77, 95% CI -1.29–-0.25,  $p < 0.05$ ) and those reporting good health status (Coef. = -0.68, 95% CI -1.16–-0.21,  $p < 0.05$ ) after ILI was smaller than that of rural residents or those reporting fair or poor health status.

## 4. Discussion

To the best of our knowledge, this is the first study using a nationally representative sample from ten provinces in China to investigate the economic burden of ILI among three high-risk groups including children, patients with chronic diseases, and the elderly. This study estimated the prevalence of self-

reported ILI, ILI-related health care seeking behaviors, the economic burden of ILI and its influencing factors among children, chronic disease patients and the elderly in China.

Despite vaccination recommendations targeted to high-risk groups and their contacts, high prevalence of ILI (45.73% of children, 16.77% of chronic disease patients and 12.70% of elderly people) was found among high-risk groups, especially among children aged 6–59 months. The results were similar to those reported in a previous study.<sup>[8]</sup> As for the health care seeking behaviors after occurring ILI, “Outpatient service only”, “OTC medication only” or “Outpatient + OTC” was most frequently chosen after ILI. At the same time, the health care seeking behaviors showed differences across the three high-risk groups. Firstly, the elderly (20.04%) were more likely to receive inpatient service than children (12.36%) and chronic disease patients (8.59%), indicating that older ILI patients were at higher risk of becoming severe cases. Secondly, larger portion of chronic disease patients (6.87%) and the elderly (6.54%) did not receive any medical services after ILI compared with children (3.35%), reflecting the problem that high-risk groups, especially the elderly and chronic disease patients, did not attach much importance to their health conditions after ILI. Consistent with a previous study in which 86% patients aged 60 years and above received ambulatory care only, and 14% were hospitalized.<sup>[11]</sup>

After the occurrence of ILI, the economic burden of the elderly was the highest (2064 yuan), followed by children (1848 yuan) and chronic disease patients (1105 yuan). It has been indicated that outpatient service and OTC medication were most frequently chosen after ILI for the three groups, but the results of medical expenses demonstrated that once inpatient service was used due to severe cases or other complications, the medical burden of ILI would be greatly increased in terms of both reimbursed expenses and self-paid expenses. A study published in 2007 estimated the medical and indirect costs attributable to annual influenza epidemics in the United States using publicly available epidemiological data, and found that indirect costs including lost productivity from missed work days and lost lives comprised even larger amount of economic burden of influenza than hospitalization costs.<sup>[18]</sup> In the present study, direct medical and non-medical costs comprised larger amount of economic burden of ILI, perhaps due to the fact that we only included lost productivity from missed work days into indirect cost.

There were several studies examining the incidence and economic burden of influenza at hospital or provincial level in China. A population-based household survey conducted in 2007 in Guangdong Province found annual ILI incidence of 49.87% among children aged 1–4 years and 2.99% among the elderly aged > 60 years, and the mean medical cost of one episode was 172.5 yuan for residents of all age groups.<sup>[8]</sup> A prospective study conducted in 2011–12 season among children younger than 5 years in Suzhou reported that the mean direct and indirect costs per episode of influenza were 777.4 yuan for outpatient clinics and 848.0 yuan for emergency departments.<sup>[9]</sup> These results were similar to the ILI incidence and economic costs reported in the present study for the three vulnerable groups. As a rough estimate, the overall annual economic burden of ILI was about 69.4 billion yuan for children, 29.0 billion yuan for chronic disease patients and 43.7 billion yuan for the elderly based on the population size recorded in statistical yearbooks.<sup>[16–17,19]</sup>



As for the co-payment of medical costs, the self-payment ratio and self-paid expenses were higher among children than chronic disease patients and the elderly due to the design of insurance schemes. Moreover, compared with children and chronic disease patients, the elderly had a lower probability of catching ILI, but higher economic burden after catching ILI. A previous study also found that young children and the elderly accounted for over 70% of the economic burden of influenza-associated hospitalizations in Jingzhou, China,<sup>[20]</sup> indicating the importance of targeted interventions such as vaccination against influenza and early treatment of ILI for high-risk groups, especially elderly people with less income and larger economic burden after ILI, as well as children with higher prevalence of ILI and higher self-payment ratio for medical expenses.

Multivariate linear regression analysis indicated that boys and the only child in the family had larger economic burden after ILI, perhaps due to the son preference and child-centered culture in some nuclear families.<sup>[21-22]</sup> As for adult respondents, it was found that urban residents had smaller economic burden than rural residents after ILI, which was consistent with some previous findings,<sup>[20]</sup> while some other studies indicated that the medical costs of influenza among urban patients were higher than those for rural patients.<sup>[7,9]</sup> Additionally, it was no wonder that for children and the elderly, the economic burden of those reporting good health status after ILI was smaller than that of those reporting fair or poor health status.

Immunization has been proven as one of the most cost-effective health investments to prevent and control influenza.<sup>[23]</sup> However, the coverage rate of influenza vaccination in China is extremely low in the past 15 years, with only 2% of the entire population being immunized.<sup>[3]</sup> Vaccination is widely recognized as an action with strong positive externalities,<sup>[24-25]</sup> so public intervention is expected to drive vaccine coverage to a socially optimal level.<sup>[26]</sup> However, as introduced above, currently, influenza vaccination has not been included in China's NIP, and the expenses are paid totally out of pocket on most occasions. Results derived from the present study on the economic burden evaluation of influenza can help raise awareness among the public health and clinical communities for the burden and consequences of this important disease. Moreover, it is crucial to support national-level decision-making on the introduction of influenza vaccination as public health project, complementary vaccination strategies and/or expanding vaccination target groups.<sup>[27]</sup>

The present study also has a few limitations. First, the economic burden reported in this study was collected from ILI cases instead of confirmed influenza cases. As recommended by WHO manuals, ILI sentinel surveillance data can be used to estimate the disease burden of influenza for specific risk groups,<sup>[28]</sup> and sentinel surveillance on ILI cases is less specific but sensitive and rapid than laboratory surveillance.<sup>[29]</sup> Therefore, it is a widely acceptable to use the results of ILI cases given that national-wide laboratory surveillance is not available at present in China, and population-based study can offer higher population representativeness than hospital surveillance data. Second, part of the elderly surveyed in this study were recruited from community health centers when they were seeking primary medical services, which may result in selection bias. Nevertheless, given the high prevalence of non-communicable chronic

diseases among Chinese elderly<sup>[30]</sup> and the fact that community health centers mainly provide primary health care, the bias can be reduced. Third, the self-reported responses may be subjected to recalling bias and a tendency to report socially desirable responses, therefore, the results should be interpreted with caution. To minimize its effect, we asked participants' most recent influenza episode. Despite these limitations, the nationally representative sample was large, with a diverse socio-demographic population, thus offering good generalizability for the three high-risk groups in China.

## 5. Conclusions

In conclusion, the prevalence of ILI was fairly high among children, chronic disease patients and the elderly during the 2018–19 influenza season in China, and most participants chose outpatient service and/or OTC medication after ILI. The results highlight the large economic burden of ILI, especially among the elderly with less income and larger economic burden after ILI, as well as children with higher prevalence of ILI and higher self-payment ratio for medical expenses. Besides, boys, the only child in the family, and urban adult residents tended to have larger economic burden after ILI. Therefore, it is important to adopt targeted interventions such as vaccination and early treatment for high-risk groups, and this study can help national-level decision-making on the introduction of influenza vaccination as public health project for the three high-risk groups.

## List Of Abbreviations

Low- and middle-income countries (LMICs)

World Health Organization (WHO)

National Immunization Program (NIP)

Influenza-like illness (ILI)

Over-the-counter (OTC)

Confidence interval (CI)

## Declarations

### Ethics approval and consent to participate

This study was approved by Peking University Institutional Review Board (IRB00001052-19076). Written informed consent was obtained from individual or guardian participants.

### Consent for publication

Not applicable.

## Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available because our informed consent form stated that the collected data would only be used for scientific research, but are available from the corresponding author on reasonable request.

## Competing interests

The authors declare that they have no competing interests.

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## Authors' contributions

H.F., L.F., X.L., H.R., X.M., Z.H., S.L. and Z.P. designed the analysis. X.L., H.R., X.M., Z.H., S.L., R.J., H.Z., Y.L., J.W. and H.F. conducted the survey and collected the data. X.L. and H.F. did the data analysis. X.L. was a major contributor in writing the manuscript. H.F., L.F., X.M., Z.H., S.L. and X.L. reviewed and edited the paper. All authors contributed to the interpretation of the results, and to the revision and final preparation of the paper for submission.

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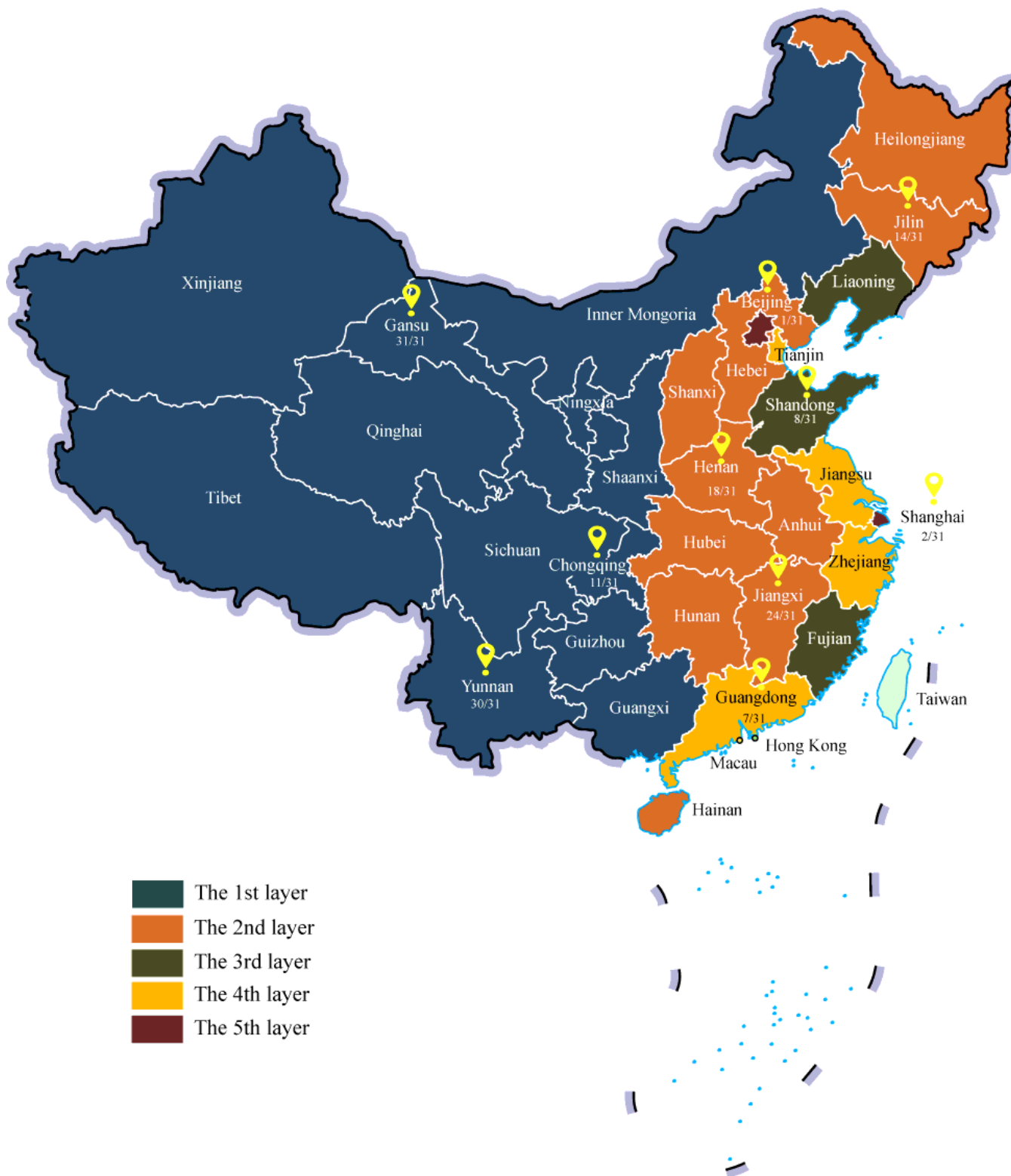
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## Figures



**Figure 1**

Ten provinces/municipalities selected for survey on the economic burden of influenza-like illness in China  
 Legend: In the survey, ten provinces/municipalities (3, 3, 1, 1, and 2 in each layer) were chosen, including Beijing, Shanghai, Jilin, Yunnan, Shandong, Guangdong, Jiangxi, Gansu, Chongqing and Henan. Their location and 2018 per capita GDP rank (e.g., 1/31) are marked in the figure. Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion

whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.