Seroprevalence of pandemic (H1N1) 2009 influenza and effectiveness of 2010/2011 influenza vaccine during 2010/2011 season in Beijing, China

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Background  In the post-pandemic period, pandemic (H1N1) 2009 virus was expected to circulate seasonally and was introduced into trivalent influenza vaccine during 2010/2011 season in the Northern Hemisphere.

Objectives  The aim of this study was to examine the evolution of herd immunity against pandemic (H1N1) 2009 virus in Beijing, China, during 2010/2011 season and effectiveness of the 2010/2011 trivalent vaccine.

Methods  Two serological surveys were conducted before and after 2010/2011 season in Beijing. A case–control study was used to investigate vaccine effectiveness against influenza-like illness (ILI) and lower respiratory tract infection (LRI).

Results  A total of 4509 and 4543 subjects participated in the pre- and post-season surveys, respectively. The standardized seroprevalence of pandemic (H1N1) 2009 influenza increased from 22% pre-season to 24% post-season (P < 0.001).

Significant elevation in seroprevalence appeared in the ≥60 years age-group (P < 0.001), but not in others. The 2010/2011 trivalent vaccine contributed to the higher post-seasonal seroprevalence in unvaccinated individuals (P = 0.024), but not in those vaccinated with monoantigenic pandemic vaccine (P = 0.205), as well as in those without prior immunity versus those with immunity. The adjusted effectiveness of the 2010/2011 trivalent vaccine was 79% protection against ILI (95% CI, 61–89%) and 95% against LRI (95% CI: 59–99%).

Conclusions  A slight increase in herd immunity against pandemic (H1N1) 2009 influenza was observed in Beijing, China, during the 2010/2011 season. Prior vaccination and immunity had a suppressive impact on immune response toward this novel influenza virus, elicited by 2010/2011 trivalent vaccine. This trivalent vaccine conferred good protection against ILI and LRI.

Keywords  Influenza vaccine, pandemic (H1N1) 2009 influenza, Seroprevalence, vaccine effectiveness.

Introduction  The first influenza pandemic in the 21st century was caused by a novel swine origin influenza virus that appeared in 2009 and affected more than 200 countries worldwide. This pandemic was relatively mild and only a small proportion of cases contracting pandemic (H1N1) 2009 virus presented with severe complications or died. Following the waning of the pandemic around the world, on August 10, 2010, the World Health Organization (WHO) announced that the world had moved into the post-pandemic period and pandemic (H1N1) 2009 virus would take on the behavior of a seasonal influenza virus.

During the pandemic period, some serological studies were conducted to determine the immunity against pandemic (H1N1) 2009 influenza in the population and indicated that the immunity differed largely by age, occupation, area, period, vaccination status, and intervention measures. These serological studies made a major contribution to our understanding of the features of this pandemic and how it developed. After entry into the post-pandemic period, the cocirculation of pandemic (H1N1)
2009 virus and the classic seasonal influenza virus was a new scenario for seasonal influenza, which might have shown an uncertain and interesting profile. A serological study was warranted to examine the epidemiology of pandemic (H1N1) 2009 influenza in the normal influenza season as well as in the pandemic.

After emergence of the novel pandemic virus in 2009, many countries initiated production of pandemic (H1N1) 2009 influenza vaccines with various formulations (non-adjuvant/adjuvant and subunit/split). These pandemic vaccines were able to elicit a sufficient immune response in clinical trials,11–14 as well as provide satisfactory protection against the disease attributed to pandemic (H1N1) 2009 virus.15–18 Thereafter, pandemic (H1N1) 2009 virus strain was recommended by WHO to be included in the 2010/2011 Northern Hemisphere trivalent influenza vaccine.19 The pandemic (H1N1) 2009 virus strain was a new member of the trivalent vaccine; therefore, the immune response induced by the new strain as well as the effectiveness of the trivalent vaccine was unknown.

To examine the seroprevalence of pandemic (H1N1) 2009 influenza in the 2010/2011 influenza season, and the immunogenicity and effectiveness of the 2010/2011 trivalent influenza vaccine, we conducted a population-based serological study in Beijing, China.

Materials and methods

Subjects and study design

This serological study consisted of two serological surveys that were launched before (September 2010) and after (April 2011) the 2010/2011 influenza season. During the pre-season period, subjects were recruited by multistage stratified random sampling technique. First, six districts were randomly selected from a total of 18 in Beijing, China; second, two communities were randomly selected in each of the six districts; and finally, 75 subjects for each age-group (0–5, 6–15, 16–24, 25–59, and ≥60 years) were recruited from each community. After obtaining informed consent from the subjects or their guardians, a questionnaire survey was administered by face-to-face interview by trained staff, and blood samples were collected for testing for antibody against pandemic (H1N1) 2009 virus. During the post-season period, the subjects participating in the pre-season survey were followed up and invited to participate in the post-season survey. For those who declined to participate, substitutes who were matched for age were randomly selected from the same community. Again, after informed consent was obtained, a questionnaire survey was undertaken by face-to-face interview, and blood samples were collected for testing for antibody against pandemic (H1N1) 2009 virus. This study was approved by the institutional review board and human research ethics committee of Beijing Center for Disease Prevention and Control (CDC).

Survey contents

The questionnaire included questions on sex, age, occupation, underlying disease, as well as history of seasonal influenza vaccination and monovalent pandemic (H1N1) 2009 influenza vaccination before the 2010/2011 influenza season. For the post-season survey, we established whether the subjects received the 2010/2011 trivalent influenza vaccine, and the occurrence of influenza-like illness (ILI) and lower respiratory tract infection (LRI) during the 2010/2011 influenza season (from October 2010 to March 2011). Influenza-like illness was defined as fever (≥38°C) plus either cough or sore throat,30 and LRI included tracheobronchitis, bronchiolitis, and pneumonia.21

Laboratory testing

Serum samples were pre-treated and assayed by hemagglutination-inhibition (HI) assay, as previously described.8,9 One volume of serum was treated with four volumes of receptor-destroying enzyme (RDE) at 37°C for 18 hours, and then incubated at 56°C for 30 minutes, followed by absorption with turkey erythrocytes. Twelve titrations (1:10, 1:20, 1:40, 1:80, 1:160, 1:320, 1:640, 1:1280, 1:2560, 1:5120, 1:10 240, and 1:20 480) were prepared for each pre-treated serum sample to test for specific antibody against pandemic (H1N1) 2009 virus antigen (A/California/07/2009) using 1% turkey erythrocytes. Immunized chicken serum samples and healthy donor blood samples harvested before the pandemic acted as positive and negative controls, respectively. The HI titer was calculated as the reciprocal of the highest dilution of serum that inhibited virus-induced hemagglutination of the turkey erythrocytes. A titer value of ≥40 was regarded as positive.8,9

Statistical analysis

Data were entered in duplicate using EpiData Software and were analyzed using SPSS11.5 statistical package (SPSS Inc., Chicago, IL, USA). We estimated the seroprevalence rates and geometric mean titers (GMTs) of antibody against pandemic (H1N1) 2009 virus before and after the 2010/2011 influenza season in all the subjects who participated in both surveys. By analyzing the data of the cohort who participated in both surveys, we assessed the effects of prior vaccination and immunity against pandemic (H1N1) 2009 influenza on seroprevalence, GMT, and seroconversion of antibody against pandemic (H1N1) 2009 influenza induced by 2010/2011 trivalent influenza vaccine in the post-season survey. We also estimated the effectiveness of 2010/2011 trivalent influenza vaccine against ILI and LRI. Prior vaccination means having ever received monovalent pandemic (H1N1)
2009 influenza vaccine in the 2009/2010 season, and prior immunity means a serum HI titer of antibody against pandemic (H1N1) 2009 virus ≥40 in the pre-season survey. Median and range values were calculated for continuous variables, and percentages for categorical variables. Seroprevalence rates of pandemic (H1N1) 2009 influenza (HI titer ≥40) were compared between subgroups using the chi-square test, and GMTs were compared using the Wilcoxon rank-sum analysis. The McNemar test was used to compare seroprevalence rates before and after the 2010/2011 influenza season in the cohort. A case–control study design was employed to estimate effectiveness of the 2010/2011 trivalent influenza vaccine against ILI and LRI in 2010/2011 influenza season. A univariate unconditional logistic regression model was used to calculate crude odds ratio (OR) of 2010/2011 trivalent influenza vaccination among subjects with ILI or LRI versus controls, and a multivariate model was used to calculate adjusted OR. Backward logistic regression was conducted by removing variables with $P > 0.10$. Vaccine effectiveness was estimated as $100 \times (1 – \text{adjusted OR})$, as described previously. All the tests were 2-sided, and statistical significance was defined as $P < 0.05$.

**Results**

**Characteristics of subjects**

A total of 4509 subjects participated in the pre-season survey, and 4543 in the post-season survey. Of 4509 subjects in the pre-season survey, 1217 (27.0%) consented to participate in the post-season survey as a cohort. The age distribution of participants involved in the pre-season survey (median: 21 years old; range: 2–102 years) was similar to that of participants in post-season survey (median: 21 years old; range: 0–92 years), as well as that of the cohort participating in both surveys (median: 22 years old; range: 1–89 years). The proportion of females in the pre-season survey was 55.5% (2504/4509), compared to 56.2% (2553/4543) in the post-season survey and 58.7% (714/1217) in the cohort participating in both surveys. Besides age and sex, the distribution of occupation was similar between the various groups (Table 1).

**Seroprevalence and GMT of antibody against pandemic (H1N1) 2009 virus in the 2010/2011 influenza season**

The seroprevalence rate of antibody against pandemic (H1N1) 2009 virus was significantly higher in the post-season than in the pre-season survey (28.4% versus 25.2%, $P < 0.001$). After taking into account the age distribution of the general population in Beijing, the standardized seroprevalence rate in the post-season group was 24.3% as opposed to 22.1% in the pre-season group ($P < 0.001$).

| Characteristics | Pre-season (September, 2010) | Post-season (April, 2011) | Cohort* |
|-----------------|-----------------------------|--------------------------|---------|
| Age-group (years) | Median (range) | 21 (2–102) | 21 (0–92) | 22 (1–89) |
| 0–5 | 647 (14.3) | 700 (15.4) | 120 (9.9) |
| 6–15 | 1118 (24.8) | 1106 (24.3) | 358 (29.4) |
| 16–24 | 844 (18.7) | 851 (18.7) | 225 (18.5) |
| 25–59 | 937 (20.8) | 947 (20.8) | 256 (21.0) |
| ≥60 | 963 (21.4) | 939 (20.8) | 258 (21.2) |
| Sex | | | |
| Male | 2005 (44.5) | 1990 (43.8) | 503 (41.3) |
| Female | 2504 (55.5) | 2553 (56.2) | 714 (58.7) |
| Occupation | | | |
| Children in family care | 242 (5.4) | 135 (3.0) | 29 (2.4) |
| Children in kindergarten | 699 (15.5) | 753 (16.6) | 140 (11.5) |
| Student | 1219 (27.0) | 1319 (29.0) | 389 (32.0) |
| Healthcare worker | 116 (2.6) | 110 (2.4) | 49 (4.0) |
| Other | 2233 (49.5) | 2226 (49.0) | 610 (50.1) |
| Total | 4509 (100) | 4543 (100) | 1217 (100) |

Data are no. (%) of subjects.

*Subjects in the cohort who participated in both surveys, that is, those who agreed to participate in the post-season survey after involvement in the pre-season one.

There was a significant difference in seroprevalence between the pre-season and post-season surveys in subjects aged ≥60 years (12.1% versus 21.2%; $P < 0.001$), but not in other age-groups. With respect to GMT, this difference was found in the subjects aged ≥60 years (8.4 versus 10.9; $P < 0.001$) as well as 0–5 years (13.1 versus 15.1; $P = 0.014$). There was a significant difference in seroprevalence (25.6% versus 31.0%; $P < 0.001$) and GMT (12.5 versus 14.7; $P < 0.001$) between the pre-season and post-season surveys for male subjects, but not in female subjects. In addition, there was no significant change in seroprevalence or GMT between the pre-season and post-season surveys in children in family care, children in kindergarten, students and healthcare workers (Table 2).

For the cohort who participated in both surveys, although seroprevalence in the pre-season survey was a little higher than that in the post-season survey, this difference was not significant (25.6% versus 24.3%; $P = 0.406$). During the 2010/2011 season, the seroconversion rate was 14.5% (177/1217).
Effects of prior vaccination and immunity against pandemic (H1N1) 2009 influenza on immunity induced by 2010/2011 trivalent vaccine

Among the subjects who never received monovalent pandemic (H1N1) 2009 influenza vaccine in the 2009/2010 season, those with 2010/2011 trivalent influenza vaccination had significantly higher seroprevalence (25.8% versus 19.0%; 𝑃 = 0.024), GMT (13.0 versus 10.0; 𝑃 = 0.007) and seroconversion rate (19.0% versus 11.4%; 𝑃 = 0.003) of antibody against pandemic (H1N1) 2009 influenza in the post-season, compared to those without vaccination. Among the subjects who had ever received monovalent pandemic (H1N1) 2009 influenza vaccine in the 2009/2010 season, those with 2010/2011 trivalent influenza vaccination did not have a significantly higher seroprevalence (45.6% versus 38.0%; 𝑃 = 0.205), GMT (24.2 versus 19.4; 𝑃 = 0.180) and seroconversion rate (20.4% versus 16.7%; 𝑃 = 0.427) of antibody against pandemic (H1N1) 2009 influenza in the post-season, compared to those without vaccination (Table 3).

Prior immunity against pandemic (H1N1) 2009 influenza had almost the same effect as prior monovalent pandemic (H1N1) 2009 influenza vaccination on seroprevalence, GMT and seroconversion rate of antibody against pandemic (H1N1) 2009 influenza induced by 2010/2011 trivalent influenza vaccine in the post-season (Table 3).

Effectiveness of 2010/2011 trivalent influenza vaccine in preventing ILI and LRI in 2010/2011 influenza season

In univariate analysis, subjects with 2010/2011 trivalent influenza vaccination had a lower risk of ILI [OR, 0.41 (95% CI, 0.24–0.73); 𝑃 = 0.002] as well as LRI [OR, 0.10 (95% CI, 0.01–0.75); 𝑃 = 0.025], compared to unvaccinated subjects. In multivariate analysis with adjustment for sex, age, occupation, underlying disease, prior immunity against pandemic (H1N1) 2009 influenza in pre-season, seasonal influenza vaccination status in the previous three influenza seasons (2007/2008, 2008/2009 and 2009/2010), and vaccination status for monovalent pandemic (H1N1) 2009 influenza vaccine, 2010/2011 trivalent influenza vaccination was consistently associated with lower probability of ILI [OR, 0.21 (95% CI, 0.11–0.39); 𝑃 < 0.001] and LRI [OR, 0.05 (95% CI, 0.01–0.41); 𝑃 = 0.005]. Therefore, 2010/2011 trivalent influenza vaccination was able to confer 79% protection against ILI (95% CI: 61–89%) and 95% protection against LRI (95% CI: 59–99%) (Table 4).

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### Table 2: Seroprevalence and GMT of antibody against pandemic (H1N1) 2009 influenza in the 2010/2011 influenza season

| Characteristics          | Seroprevalence |               | GMT*          |               |          |
|--------------------------|----------------|---------------|---------------|---------------|----------|
|                          | Pre-season     | Post-season   | 𝑃-value**     | Pre-season    | Post-season | 𝑃-value*** |
|                          | (September, 2010) | (April, 2011) |               | (September, 2010) | (April, 2011) |          |
| Age-group (years)        |                |               |               |               |           |
| 0–5                      | 184/647 (28.4) | 228/700 (32.6) | 0.100         | 13.1         | 15.1      | 0.014     |
| 6–15                     | 370/1118 (33.1)| 403/1106 (36.4)| 0.098         | 15.9         | 17.2      | 0.737     |
| 16–24                    | 286/844 (33.9) | 268/851 (31.5) | 0.293         | 16.8         | 15.3      | 0.536     |
| 25–59                    | 178/937 (19.0) | 190/947 (20.1) | 0.559         | 10.1         | 10.2      | 0.990     |
| ≥60                      | 119/963 (12.4) | 199/939 (21.2) | <0.001        | 8.4          | 10.9      | <0.001    |
| Sex                      |                |               |               |               |           |
| Male                     | 514/2005 (25.6)| 617/1990 (31.0)| <0.001        | 12.5         | 14.7      | <0.001    |
| Female                   | 623/2504 (24.9)| 671/2553 (26.3)| 0.253         | 12.3         | 12.6      | 0.627     |
| Occupation               |                |               |               |               |           |
| Children in family care  | 66/242 (27.3) | 38/135 (28.1) | 0.855         | 12.4         | 13.2      | 0.111     |
| Children in kindergarten | 195/699 (27.9)| 245/753 (32.5)| 0.055         | 13.1         | 15.2      | 0.089     |
| Student                  | 459/1219 (37.7)| 492/1319 (37.3)| 0.854         | 18.6         | 17.9      | 0.277     |
| Healthcare worker        | 43/116 (37.1) | 45/110 (40.9) | 0.554         | 17.2         | 17.7      | 0.793     |
| Other                    | 374/2233 (16.7)| 468/2226 (21.0)| <0.001        | 9.6          | 10.8      | 0.001     |
| Total                    | 1137/4509 (25.2)| 1288/4543 (28.4)| 0.001         | 12.4         | 13.5      | 0.007     |

GMT, geometric mean titer. Data from all participants in pre-season and post-season surveys were included in this analysis. Data are seropositive no./total no. in each group (%), unless otherwise indicated.

*Titers of antibodies against hemagglutinin below the lower limit (1:10) were determined a value of 1:5 for calculating GMT.

**Compared by the chi-square test.

***Compared by Wilcoxon rank-sum test.
Immunity and vaccine effectiveness against H1N1

Table 3. Effects of prior vaccination and immunity against pandemic (H1N1) 2009 influenza on immunity against pandemic (H1N1) 2009 influenza induced by 2010/2011 trivalent influenza vaccine in the post-season survey

| Characteristics | Receipt of 2010/2011 trivalent influenza vaccine | Seroprevalence* | P-value** | GMT*** | P-value† | Seroconversion rate‡+ | P-value** |
|----------------|-----------------------------------------------|-----------------|-----------|--------|----------|----------------------|----------|
| Characteristics in pre-season of 2010/2011 influenza season (September, 2010) | | | | | | | |
| Prior vaccination*†† | Yes | Yes | 47/103 (45:6) | 0.025 | 24.2 | 0.018 | 21/103 (20.4) | 0.427 |
| | No | Yes | 73/192 (38:0) | 0.024 | 13.0 | 0.007 | 47/248 (19:0) | 0.003 |
| | No | No | 128/674 (19:0) | 10.0 | 77/674 (11:4) | | |
| Prior immunity‡ | Yes | Yes | 42/91 (46:2) | 0.734 | 24.4 | 0.802 | 5/91 (5:5) | 0.564 |
| | No | Yes | 99/205 (48:3) | <0.001 | 13.4 | <0.001 | 63/260 (24:2) | <0.001 |
| | No | No | 102/661 (15:4) | 9.0 | 94/661 (14:2) | | |

GMT, geometric mean titer; HI, hemagglutination-inhibition.

Data from 1217 subjects who participated in both pre-season and post-season surveys were included in this analysis.

*Data are seropositive no./total no. in each group (%).

**Compared by the chi-square test.

***Titers of antibodies against hemagglutinin below the lower limit (1:10) were determined a value of 1:5 for calculating GMT.

†Compared by the Wilcoxon rank-sum test.

‡Seroconversion was defined as a 4-fold or greater increase in antibody titer of the subject between pre-season and post-season.

††Prior vaccination means having ever received monovalent pandemic (H1N1) 2009 influenza vaccine in the 2009/2010 season.

‡‡Prior immunity means a serum HI titer of antibody against pandemic (H1N1) 2009 virus ≥40 in the pre-season survey.

Discussion

Our study provides a new insight into pandemic (H1N1) 2009 influenza which appeared for the first time as seasonal influenza during the northern hemisphere influenza season. The seroprevalence rate of antibody against pandemic (H1N1) 2009 influenza was approximately 24.3% in the general population of Beijing after the 2010/2011 influenza season, which was significantly higher than 22.1% before. Prior monovalent pandemic (H1N1) 2009 influenza vaccination and prior immunity against pandemic (H1N1) 2009 influenza had an inhibitory effect on the immune response elicited by 2010/2011 trivalent influenza vaccine. Moreover, 2010/2011 trivalent influenza vaccine provided a good protection against ILI and LRI during the 2010/2011 influenza season.

In January 2010, a prior cross-sectional serological survey conducted in Beijing showed that around 29.0% of the general population was seropositive to pandemic (H1N1) 2009 influenza.9 After the activity of pandemic (H1N1) 2009 influenza decreased or even disappeared over 8 months, this figure descended to 22.1% in September, 2011, as the result of reduced immunity against pandemic (H1N1) 2009 influenza over time.12 Although the antibody level against pandemic (H1N1) 2009 influenza after the 2010/2011 influenza season was significantly greater than before, this elevation was much lower than expected.

It was of concern that there was a significantly increase in immunity against pandemic (H1N1) 2009 influenza after the 2010/2011 influenza season in the 0–5 years (GMT) and ≥60 years (seroprevalence and GMT) groups. Given the free influenza vaccination campaign among school children and the elderly in Beijing, it was assumed that vaccination was the predominant factor for the increase in the ≥60 years age-group, but infection was responsible in the 0–5 years group. In subjects aged 6–15 years, seroprevalence rate during the pre-season survey remained at 33.1%, which was almost three times that seen in the ≥60 years age-group. Although the 6–15 years group was also covered by the influenza vaccination campaign, there was no post-season increase in immunity against pandemic (H1N1) 2009 influenza, as observed in the ≥60 years group. This might be explained by the effect of prior immunity against pandemic (H1N1) 2009 influenza on 2010/2011 trivalent influenza vaccination, as follows.

It was of interest that, after 2010/2011 trivalent influenza vaccination, there was a significant increase in immunity against pandemic (H1N1) 2009 influenza in subjects without monovalent pandemic (H1N1) 2009 influenza vaccination.
or prior immunity against pandemic (H1N1) 2009 virus, compared with subjects with these exposures.

This finding put forward the possibility that pre-existing antibody against pandemic (H1N1) 2009 virus may suppress the humoral immune response of 2010/2011 trivalent influenza vaccine, by a negative feedback. This inhibitory effect of baseline antibody on B-cell response elicited by vaccination has been observed for other viruses.23–26

We showed that, during the 2010/2011 influenza season, there was a significant increase in the level of antibody against pandemic (H1N1) 2009 virus in the male but not the female population of Beijing. This difference indicated that there were more cases of influenza in males than in females, although they had similar coverage rates of influenza vaccination (data not shown). This might be because females were more likely to follow recommended behaviors for preventing pandemic (H1N1) 2009 influenza.27

Because of the greater difficulty in collecting paired blood samples from the 0–5 years than the other age groups, the proportion of subjects aged 0–5 years among the cohort that participated in both surveys was much less than that among all the participants of the pre-season and post-season surveys. There was a significant increase in antibody level in the 0–5 years age-group among all the participants during the 2010/2011 influenza season (Table 2). Therefore, the lower proportion of subjects aged 0–5 years among the cohort participating in both surveys would have affected the overall antibody level of the cohort after the 2010/2011 season. Thus, a significant difference was found in seroprevalence rates between the pre-season and post-season surveys in all participants, but was not found in the cohort that participated in both surveys.

Monovalent pandemic (H1N1) 2009 influenza vaccine gave good protection against infection with pandemic (H1N1) 2009 virus, which has been validated by some observational studies.15–18 However, the effectiveness of 2010/2011 trivalent influenza vaccine urgently needs evaluation after inclusion of the pandemic (H1N1) 2009 influenza hemagglutination antigen. A couple of studies have evaluated the effectiveness of the trivalent vaccine in the middle of the 2010/2011 influenza season.28,29 In the present study, we conducted a comprehensive evaluation on the effectiveness of 2010/2011 influenza vaccination for the entire influenza season and demonstrated that this new trivalent vaccine provided good protection against ILI and LRI, which were strongly associated with influenza during the influenza season.30 Given that H3N2 and pandemic (H1N1) 2009 viruses played a dominant role alternatively during the 2010/2011 influenza season, it was assumed that 2010/2011 influenza vaccination could confer protection against infection with both viruses.

Some serological studies have shown that seroprevalence rates of antibody against pandemic (H1N1) 2009 virus after monovalent pandemic (H1N1) 2009 influenza vaccination in large campaigns were much lower than those found in clinical trials.8,9,14,15,31 This indicates that persistence of humoral immunity elicited by monovalent pandemic (H1N1) 2009 influenza vaccine is not satisfactory. In the 2010/2011 influenza season, the pandemic (H1N1) 2009 virus component was incorporated into the trivalent influenza vaccine, and this trivalent vaccine did not induce a

### Table 4. Effectiveness of 2010/2011 trivalent influenza vaccine in preventing ILI* and LRI** in the 2010/2011 influenza season

| Group   | Case     | Control  | Crude OR (95% CI), P-value† | Adjusted OR (95% CI), P-value† | Vaccine effectiveness (95% CI)††† |
|---------|----------|----------|----------------------------|---------------------------------|----------------------------------|
|         | Yes (10%) (47) | Yes (47) | 0.41 (0.24–0.73) | 0.21 (0.11–0.39) | 79% (61–89%) |
|         | No (53)  | No (53)  | 0.002                     | <0.001                          | 95% (59–99%) |

ILI, influenza-like illness; LRI, lower respiratory tract infection.

Data from 1217 subjects who participated in both pre-season and post-season surveys were included in this analysis. Data are proportion (%), unless otherwise indicated.

*Fever (≥38°C) plus either cough or sore throat.

**Including tracheobronchitis, bronchiolitis, and pneumonia.

***Vaccination with 2010/2011 trivalent influenza vaccine.

† Obtained by univariate logistic regression model.

†† Obtained by multivariate logistic regression model after adjustment for sex, age, occupation, underlying disease, prior immunity against pandemic (H1N1) 2009 influenza in pre-season, seasonal influenza vaccination status in the previous three influenza seasons (2007/2008, 2008/2009, and 2009/2010) and vaccination status for monovalent pandemic (H1N1) 2009 influenza vaccine.

††† Calculated as 100 × (1 – adjusted OR).
 persistent antibody level against pandemic (H1N1) 2009 influenza for the entire season. This phenomenon may be because pandemic (H1N1) 2009 influenza is an emerging virus, which has not yet established efficient B-cell memory, and thus vaccination against pandemic (H1N1) 2009 influenza does not induce strong and durable humoral immunity. The inability to elicit persistent antibody against pandemic (H1N1) 2009 virus and the effectiveness of monovalent and trivalent influenza vaccines suggests that cell-mediated immunity, which has been shown to appear after influenza vaccination, plays a crucial role in protection against pandemic (H1N1) 2009 influenza.

This study had several limitations. First, some data were self-reported, which could have led to problems with recall bias. Second, only a proportion of subjects who participated in the pre-season survey agreed to participate in the post-season survey. Therefore, the cohort included in the analysis might not have represented the initial subjects enrolled in the pre-season survey, which could possibly have introduced selection bias. Nonetheless, considering the similarity of the demographic characteristics of the cohort compared with all the subjects in the pre-season survey, we think that this selection bias would have been limited. Third, this study was a sampling survey, which will inevitably have had sampling bias. However, because the participants were selected from communities by strict random sampling, they do represent well the general population of Beijing.

Our study suggests that a slight increase in antibody level against pandemic (H1N1) 2009 influenza was observed in Beijing, China, after the 2010/2011 influenza season. Prior vaccination and immunity against pandemic (H1N1) 2009 influenza had an inhibitory impact on the humoral immune response toward this novel influenza virus elicited by 2010/2011 trivalent influenza vaccine. This trivalent vaccine conferred good protection against ILI and LRI during the influenza season.

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Author contributions

Dr Peng Yang contributed to study design, implementation, data analysis, and writing of paper. Dr Li Zhang is a project manager involved in form development and data analysis. Dr Weixian Shi contributed to study design and involved in laboratory technical assistance. Dr Guilan Lu and Dr Xiaomin Peng involved in laboratory testing and drafting of paper. Dr Shujuan Cui contributed to database development and statistical analysis. Dr Daitao Zhang involved in laboratory testing and analysis. Dr Yimeng Liu contributed to database management and analysis. Dr Huijie Liang involved in statistical analysis and drafting of paper. Dr Xinghuo Pang contributed in recruitment and training. Professor Quanyi Wang contributed to study design, implementation, overseeing the whole study, data analysis, and writing of paper.

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