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Economic burden of influenza illness among children under 5 years in Suzhou, China: Report from the cost surveys during 2011/12 to 2016/17 influenza seasons

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Abstract

Background: Data are limited on the economic burden of seasonal influenza in China. We estimated the cost due to influenza illness among children < 5-year-old in Suzhou, China.

Methods: This study adopted a societal perspective to estimate direct medical cost, direct non-medical cost, and indirect cost related to lost productivity. Data to calculate costs and rates of three influenza illness outcomes (non-medically attended, outpatient and hospitalization) were collected from prospective community-based cohort studies and hospital-based enhanced laboratory-confirmed influenza surveillance in Suzhou during the 2011/12 to 2016/17 influenza seasons. We used mean cost-per-episode, annual incidence rates of episodes of each outcome, and annual population size to estimate the total annual economic burden of influenza illnesses among children < 5-year-old for Suzhou. All costs were reported in 2017 U.S. dollars.

Results: The mean cost-per-episode (standard deviation) was $9.92 (13.26) for non-medically attended influenza, $161.05 (176.98) for influenza outpatient illnesses, and $1425.95 (603.59)

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the U.S. Centers for Disease Control and Prevention.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2020.12.075.

for influenza hospitalizations. By applying the annual incidence rates to the population size, we estimated an annual total of 4,919 episodes of non-medically attended influenza, 21,994 influenza outpatient, and 2,633 influenza hospitalization. Total annual economic burden of influenza to society among children < 5-year-old in Suzhou was $7.37 (95% confidence interval, 6.9–7.8) million, with estimated costs for non-medically attended influenza of $49,000 (46,000–52,000), influenza outpatients $3.5 (3.3–3.8) million, and influenza hospitalizations $3.8 (3.6–3.9) million. Among outpatients, the indirect cost was 36.3% ($1.3 million) of total economic burden, accounting for 21,994 days of lost productivity annually. Among inpatients, the indirect cost was 22.1% ($829,000), accounting for 18,431 days of lost productivity annually.

Conclusions: Our findings show that influenza in children < 5-year-oldcauses substantial societal economic burden in Suzhou, China. Assessing the potential economic benefit of increasing influenza vaccination coverage in this population is warranted.

Keywords

Influenza; Children; Economic burden; China; Direct cost; Indirect cost

1. Introduction

Annual influenza epidemics result in 3–22 million cases of severe illness worldwide [1]. During seasonal influenza epidemics, excess pneumonia and influenza hospitalizations of 3–4 per 1,000 children in the United States of America (U.S.) and excess cardiopulmonary outpatient visits of 6–15 per 100 children in children < 5-years-old in China have been observed annually [2–4]. Laboratory-confirmed influenza surveillance in the U.S. and China suggests hospitalization rates in children < 5-year-old ranged from 3 to 23 per 1,000 children annually, which is comparable to that in elderly populations [5,6].

Studies have shown that influenza infection in children carries significant direct medical costs but also results in significant indirect economic costs due to loss of productivity among caregivers [7–10]. However, data on the economic burden of influenza among children <5-year-old in China are limited. Previous studies which focused on outpatient and/or hospitalization did not include non-medically attended influenza [11] nor did they report indirect cost outcomes [12–15]. Understanding economic burden of influenza is important for understanding the cost effectiveness and economic benefit of influenza vaccination programs. In part, the lack of these data in China limits the expansion of influenza vaccination programs in children < 5 years such that influenza vaccination coverage in this population was estimated at < 30% from 2009 to 2016 [16,17]. We estimated the economic burden of seasonal influenza among children < 5-years during the 2011/12 to 2016/17 influenza seasons in Suzhou, China—a city of approximately 10 million population in eastern China.

2. Methods

2.1. Influenza surveillance

Laboratory-confirmed influenza surveillance was conducted at Suzhou University Affiliated Children’s Hospital (SCH), the only tertiary hospital for children in Suzhou. SCH is a

1400-bed hospital that has estimated 1.5 million outpatient and 42,000 inpatient visits annually [18]. The hospital is accessible to all children regardless of Suzhou residency status, and based on previous studies, the catchment area for SCH has been defined as the five municipal districts in Suzhou [19].

From 1 October 2011–30 September 2017, we conducted year-round influenza-like illness(ILI) and severe acute respiratory illness (SARI) surveillance among children in the outpatient clinics and inpatient wards at SCH. Methods for surveillance at SCH have been previously described [19,20]. In brief, all children < 5-year-old who resided in the catchment area for longer than 6 months who presented to SCH within 7 days of symptom onset were eligible for enrollment. Respiratory specimens were collected from all eligible children who presented to the designated physicians within 3 days of symptom onset. Viral RNA was extracted using high pure viral RNA kits (Roche, Shanghai, China). Real-time reverse transcription polymerase chain reaction (rtRT-PCR) was employed to test for influenza using influenza virus dual fluorescent quantitative RT-PCR kits (Bio Perfectus Technology Co., Jiangsu, China) as described previously [19,20]. We defined an influenza season as 1 October in one year to 30 September in the following year [21].

2.2. Study perspective

This study adopted a societal perspective, including direct medical and non-medical costs and indirect costs, and we considered cost burden associated with three influenza illness outcomes: non-medically attended illness, outpatient illness, and hospitalization.

2.3. Cost calculation

Direct medical costs included any applicable items for each illness outcome from cost categories of over the counter (OTC) medications and for outpatient illnesses and hospitalizations, charged costs of diagnostic, therapeutic, supplies/room and physician services incurred during a visit to clinic or hospital.

Direct non-medical costs included any applicable items for each illness outcome from cost categories of food, transportation, caregiver's lodging and nutrition supplementation incurred as a result of the influenza illness. The cost of food, lodging and nutrition supplementation were provided directly by caregiver interviews. For transportation, if the respondents could not recall the exact costs, we used the drive distance in kilometers from home to hospital obtained from Baidu Map and applied an estimated unit cost of 9.02 USD per 100 km, assuming fuel consumption of 7.5L/100 km and fuel price at 1.2 USD/L.

Indirect costs were associated with lost productivity of family members to care for the sick child. We used the human capital method to estimate the cost of lost productivity. If caregivers were members of the labor force, lost wages were calculated by the number of days absent from work multiplied by the average daily wage in Suzhou (Supplemental Table 1) [23]. If caregivers were not members of the labor force (retired or unemployed), lost wages were calculated by the number of days caring sick child multiplied by the average daily wages of nanny labor in Suzhou (Supplemental Table 1) [23].

All costs were reported in 2017 U.S. dollars (1 USD = 6.65 RMB), adjusted for inflation using the price index of medical service [24].

2.4. Estimation of cost-per- episode of non-medically attended influenza

For non-medically attended influenza, only direct costs from the purchase of over the counter (OTC) medications were considered. Data on OTC drug cost were collected from prospective cohort studies of children 6–59 months enrolled in public and private nursery schools from different locations throughout Suzhou during the 2014/15 and 2016/17 influenza seasons [22,25]. The school teachers screened all students each school day for ILI symptoms (measured axillary temperature ≥ 38°C and cough or sore throat/inflamed or red pharynx in the preceding 7 days). For all ILI cases, parents were contacted by telephone related to health-seeking behaviors. For non-medically attended ILI cases, the cost of OTC medications was collected. For this analysis, we assumed no difference in costs between influenza- and non-influenza associated ILI and that the OTC drug cost for children < 6 months was equivalent to the OTC drug cost for children 6–59 months.

2.5. Estimation of cost-per-episode of outpatient influenza

The direct medical costs were obtained from the hospital information system (HIS) from laboratory-confirmed influenza outpatients. The direct non-medical costs and the number of days lost due to childcare and employment status of caregivers (indirect costs) were collected through caregiver telephone interviews within one week of clinic visit.

2.6. Estimation of cost-per-episode of hospitalization

We used the same methods to collect direct medical, direct non-medical, and indirect costs for laboratory-confirmed influenza hospitalizations as we did for collecting influenza outpatient cost data.

2.7. Estimation of number of influenza illness outcomes

We estimated the average annual rate of influenza outpatient and influenza hospitalization based on the observed number of laboratory-confirmed influenza ILI and influenza SARI and the healthcare seeking behavior of ILI case in SCH catchment area as described previously [19,20]. The total numbers of influenza outpatient and influenza hospitalization events in Suzhou were calculated through multiplying rates of influenza outpatient and influenza hospitalization by the size of population of children < 5-year-old in the expanded immunization program database which includes all children living in Suzhou (Supplemental Table 1).

To estimate the number of non-medically attended influenza illnesses, we multiplied the number of outpatient influenza illnesses by the ratio of non-medically attended influenza to outpatient ILI. The ratio used was derived from previously published health utilization surveys conducted in 2012/13 to 2013/14 influenza seasons among community-dwelling children <5-year-old in Suzhou [19]. We assumed that influenza-associated ILI and non-influenza-associated ILI would result in similar health utilization behaviors.

2.8. Estimation of total economic burden in Suzhou

Total influenza-associated direct costs in Suzhou were calculated from the estimated annual number of outcomes (e.g. annual number of influenza outpatient) multiplied by the cost-perepisode (e.g. cost-per-influenza outpatient). Total influenza associated indirect costs in Suzhou were calculated by the estimated total days of lost work for care of a sick child multiplied by the value of lost time based on the human capital approach [24].

2.9. Statistical analysis

We estimated the mean cost-per-episode [26] using simulation mean of bootstrap samples with 10,000 replications and calculated the standard deviation (SD) of the bootstrap samples. All cost estimations were divided into four age groups: 0–5 months, 6–23 months, 24–35 months and 36–59 months. We compared the cost of each outcome by age group, Suzhou Hukou (a household registration record, which identifies a person as a permanent resident and establishes eligibility for social programs including local government insurance), comorbidity (including congenital heart disease, asthma and other chronic lung disease, neuromuscular disease, kidney disease, blood dyspraxia and HIV) and influenza season using the Kruskall-Wallis Test. The 95% confidence interval (CI) of the estimated number of outcomes and the total cost was estimated by bootstrapping with 10,000 replications. Data analysis was performed using R, version 3.2.3 (R Foundation for Statistical Computing, Vienna, Austria).

This study was approved by the Institutional Review Board (IRB) of the School of Public Health, Fudan University, and was reviewed by the U.S. Centers for Disease Control and Prevention (CDC).

3. Results

3.1. Characteristics of participants of cost surveys

We included 2,171 children aged 6–59 months who had non-medically attended influenza (Supplemental Figure). Of those, 52.3% were male, 72.0% were aged 36–59 months, 44.1% had a Suzhou Hukou, and 1.4% had comorbidity (Table 1).

We identified a total of 836 children < 5-year-old with laboratory-confirmed influenza at outpatient clinics and 799 contributed data to estimate the cost-per-influenza outpatient (Supplemental Figure). Of the 799, 58.3% were male, 39.2% were aged 6–23 months, 63.7% had Suzhou Hukou, and 4.0% had comorbidity. The median number of lost productivity days of the caregiver was 0 day (IQR 0–2) (Table 1).

We identified a total of 440 children < 5-year-old hospitalized with laboratory-confirmed influenza and 436 contributed data to estimate the cost-per-influenza hospitalization (Supplemental Figure). Of the 436, 62.4% were male, 43.8% were aged 6–23 months, 72.0% had Suzhou Hukou, and 8.7% had comorbidity. The median length of hospitalization was 7 days (IQR 6–8), and the median number of lost productivity days of the caregivers was 7 days (IQR 6–9) (Table 1).

3.2. Cost-per-episode by influenza illness outcomes

The mean direct cost (OTC) was $9.92 (SD 13.26). No differences in cost-per-non-medically attended influenza were found based on age group or Hukou status. Children with comorbidities had higher cost-per-episode than those without ($13.95 vs. $9.74, p = 0.009) (Table 2).

The cost-per-influenza outpatient was $161.05 (176.98). The most expensive cost category was indirect medical cost at $58.49 (62.38), following by direct medical cost at $47.90 (54.81). There were statistically significant differences among different age groups in direct cost. Direct costs were higher in children with Suzhou Hukou compared to those without Suzhou Hukou and were higher in children with comorbidities compared to those with comorbidities. All cost categories of influenza outpatient varied by influenza seasons significantly (Table 2).

The cost-per-influenza hospitalization was $1425.95 (603.59). The direct medical cost was the largest category at $1000.89 (419.20), followed by indirect cost at $314.99 (272.31). Direct costs were higher in children with comorbidities compared to those without comorbidities. Children without Suzhou Hukou had a higher direct cost for influenza hospitalization than children with Suzhou Hukou. All cost categories of influenza hospitalization varied significantly by influenza seasons (Table 2).

Additional detail on the categories of the costs were shown in the Supplemental Table 3.

3.3. Number of influenza illness outcomes

The average incidence rate per 100 person-years (95% CI) was 1.67 (1.66–1.69) for non-medically attended influenza, 7.49 (7.45–7.53) for influenza outpatient, and 0.90 (0.88–0.91) for influenza hospitalization. Applying the rates to the population, we estimated that, among children < 5-year-old in Suzhou, there were 4,919 (4,864–4,975) non-medically attended influenza, 21,994 (21,880–22,108) influenza outpatient and 2,633 (2,592–2,674) influenza hospitalization outcomes annually (Table 3).

3.4. Total economic burden in Suzhou

The total annual economic burden of influenza in Suzhou was $7.3 (95% Cl: 6.9–7.8) million including $49,000 (46,000–52,000) for non-medically attended influenza, $3.5 (3.3–3.8) million for influenza outpatient, and $3.8 (3.6–3.9) million for influenza hospitalization outcomes. Among outpatients, the indirect cost accounted for 36.3% ($1.3 million) of the total economic burden, as a result of 21,994 days of lost caregiver productivity annually, followed by the direct medical cost (29.8%, $1.1 million). Among inpatients, direct medical costs accounted for 70.2% ($2.6 million) of total economic burden, followed by the indirect cost (22.1%, $0.8 million), as a result of 18,431 days of lost caregiver productivity annually. The indirect cost share was highest among children aged 0–5 months, with 43.3% ($0.06 million) in outpatient and 24.1% ($0.15 million) in inpatient outcomes (Table 4).

4. Discussion

Our study provides a comprehensive estimate of the economic impact of medically and non-medially attended influenza among children < 5-year-old 5 in Suzhou China. We estimated that the mean cost-per-episode was $9.92 for non-medically attended influenza, $161.05 for outpatient visits, and $1425.95 for hospitalizations. Total annual economic burden among children < 5-year-old in Suzhou associated with influenza was $7.3 million, of which $3.5 million was for outpatient visits and $3.8 million was for influenza hospitalizations. The indirect cost share accounted for ~ 22–36% of the total annual economic burden for inpatient and outpatient visits.

The mean cost-per-episode for influenza hospitalization was eight times as high as for an outpatient visit. Similar observations of inpatient and outpatient costs have been reported among children in other countries, such as Kenya (US$114 vs. US$21) [27], Thailand (US$232–318 vs. US$22–25) [28], and the U.S. (US$6,415 vs. US$128) [29]. As expected, the high frequency of outpatient visits increased the overall share of those events to the annual economic burden relative to the less frequent hospitalization episodes. Overall, the mean cost-per-episode in Suzhou was higher compared to that in other low and middle income countries such as Kenya and Thailand, but lower than developed countries like U.S. and Italy, which is likely attributable to differentials in healthcare pricing in those settings [27–30].

The indirect cost related to lost productivity days for caregivers account for ~ 22% total inpatient costs and ~ 36% total outpatient costs annually, and this indirect cost was as high as ~ 24% and ~ 43% of the total cost in the children aged 0–5 months. The indirect cost fraction in our study population was lower than another report from Kenya which reported indirect costs fractions of 65% in outpatients and 34% in inpatients [27]. One possibility for this difference is that in China, children are often cared for by retired grandparents, thus reducing the need for working parents to provide care during their children's illness.

Overall, a single episode of hospitalization represents 200% and outpatient represents 27% of per-capita disposable monthly income in Suzhou (US$600). Per local insurance policies for covered services, up to 25% hospitalization costs and 40% of outpatient costs would be borne by the household and the remainder by the government [31]. However, eligibility for local insurance is related to having a Suzhou Hukou. This system may create added burdens for families of children without a Suzhou Hukou especially for expensive inpatient encounters since these healthcare costs would have to be paid out of pocket thus raising the family costs for influenza illness in a system stratified by residency status. Additionally, our estimates demonstrate that influenza in children <5-year-old in Suzhou has a large economic burden for society. Indeed, we found that the direct medical costs (1.1 million for outpatients and 2.6 million for inpatients) in children < 5-year-oldmay account for ~ 10% of Suzhou's $35.5 million healthcare expenditures for that population in 2017 [31]. Given the differences in insurance coverage by Hukou status, the negative economic effects of a child infected with influenza could be particularly grim for a socioeconomically disadvantaged family.

Our cost-per-episode of influenza among children < 5-year-old differs from those found in other studies in China. Using a telephone survey of 266 pediatric influenza patients, Yang et al found a cost per episode of influenza of $214 for outpatient visits and $1644 for influenza hospitalizations in 2017 dollars, which was higher than our estimates [11]. Unlike in Yang et al which relied on data from a single influenza season and asked participants to recall medical costs from the previous 12 months [11], our results are strengthened because they represent data collected prospectively across multiple influenza seasons and avoided recall bias by collecting medical cost information from HIS records and other cost information within one week of the patient encounter. Zhou et al estimated that the cost-per-influenza outpatient visit was $11.28 and inpatient visit was $284.44 in children aged 6 months to 14 years [14,15]. While these costs were lower than the ones we described, Zhou et al's analysis did not account for patient co-payments, direct non-medical costs, and indirect costs due to lost productivity. As was shown in our study, the indirect cost due to lost caregiver productivity was high when accounting for annual economic burden of influenza in children < 5-year-old. Data on the economic burden of infectious diseases in China are limited; however, the cost-per-influenza hospitalization was higher than the cost-per-measles hospitalization of $450 when adjusted to 2017 USD [32]. Understanding these estimates is critical and the full spectrum of economic burden is essential for developing an economic justification for an influenza vaccination program.

Similar to other areas in China, the vaccination coverage in Suzhou among children aged 6–59 months was low [17,33]. In fact, in Suzhou, during our study period vaccination coverage decreased from 20% in 2011/12 to 6% in 2015/16 in children 6–59 months [33], which was likely related to a policy change that disallowed points of vaccination from setting prices for non-immunization program vaccination services thus reducing the amount of service fees collected from providing those types of vaccination including influenza vaccination [34]. A study in Suzhou among children 6–59 months by Zhang et al found that even with an average influenza vaccination coverage of 9%, approximately 7% of expected influenza illnesses and 6% of expected influenza hospitalizations would have been prevented [33]. In sensitivity analysis, if vaccination coverage increased to 50%, approximately 29% of influenza illnesses and 27% of influenza hospitalizations would have been prevented [33]. Based on these findings of averted illnesses due to influenza vaccination, increasing influenza vaccination coverage in children 6–59 months would be expected to reduce the total cost burden attributable to influenza in this population in Suzhou.

Our study has several limitations. First, the disease and economic burden may be underestimated, as the secondary infections caused by influenza virus were not captured by disease burden surveillance. Additionally, our estimations of the economic burden of non-medically attended illnesses may have been affected because our use of ILI may not have included the full spectrum of respiratory and non-respiratory influenza illnesses [36]. Second, our results are from Suzhou only. The economic burden in other areas of China may differ depending upon the patient's health-seeking and health provider's behavior. Third, our data on direct medical charges reflects hospital charges, and our data did not allow us to differentiate costs paid by health insurance versus by the patient. Fourth, the study was not designed to explain what drove the differences in unit cost by age, comorbidity or season. Fifth, we used the human capital approach to estimate the cost of productivity

which may overestimate the indirect cost compared to other methods. Finally, we did not have data on the costs of non-medically attended illness in children 0–5 months and made our calculations by assuming that their OTC medication costs would be equivalent to that of non-medically attended influenza in children 6–59 months.

In conclusion, our findings show that influenza in children < 5-year-old causes substantial societal economic burden in Suzhou, China. Assessing the potential economic benefit of influenza vaccination program in this population is warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

[1]. GBD. Mortality, morbidity, and hospitalisations due to influenza lower respiratory tract infections, 2017: an analysis for the Global Burden of Disease Study 2017. The Lancet Respiratory medicine. 2019;7:69–89. [PubMed: 30553848]

[2]. Thompson WW, Shay DK, Weintraub E, Brammer L, Bridges CB, Cox NJ, et al. Influenza-associated hospitalizations in the United States. JAMA 2004;292:1333–40. [PubMed: 15367555]

[3]. Neuzil KM, Mellen BG, Wright PF, Mitchel EF Jr. Griffin MR. The effect of influenza on hospitalizations, outpatient visits, and courses of antibiotics in children. New England J Med 2000;342:225–31. [PubMed: 10648763]

[4]. Zhang X, Zhang J, Chen L, Feng L, Yu H, Zhao G, et al. Pneumonia and influenza hospitalizations among children under 5 years of age in Suzhou, China, 2005–2011. Influenza Other Respir Viruses 2017;11:15–22. [PubMed: 27383534]

[5]. Neuzil KM, Zhu Y, Griffin MR, Edwards KM, Thompson JM, Tollefson SJ, et al. Burden of interpandemic influenza in children younger than 5 years: a 25-year prospective study. J Infect Dis 2002;185:147–52. [PubMed: 11807687]

[6]. Yu H, Huang J, Huai Y, Guan X, Klena J, Liu S, et al. The substantial hospitalization burden of influenza in central China: surveillance for severe, acute respiratory infection, and influenza viruses, 2010–2012. Influenza Other Respir Viruses 2014;8:53–65. [PubMed: 24209711]

[7]. Molinari NA, Ortega-Sanchez IR, Messonnier ML, Thompson WW, Wortley PM, Weintraub E, et al. The annual impact of seasonal influenza in the US: measuring disease burden and costs. Vaccine 2007;25:5086–96. [PubMed: 17544181]

[8]. Turner D, Wailoo A, Nicholson K, Cooper N, Sutton A, Abrams K. Systematic review and economic decision modelling for the prevention and treatment of influenza A and B. Health technology assessment (Winchester, England). 2003;7:iii-iv, xi-xiii, 1–170.

[9]. Esposito S, Gasparini R, Bosis S, Marchisio P, Tagliabue C, Tosi S, et al. Clinical and socio-economic impact of influenza and respiratory syncytial virus infection on healthy children and their households. Clin Microbiol Infect Off Publicat European Soc Clin Microbiol Infect Dis 2005;11:933–6.

[10]. Li S, Leader S. Economic burden and absenteeism from influenza-like illness in healthy households with children (5–17 years) in the US. Respir Med 2007;101:1244–50. [PubMed: 17156991]

[11]. Yang J, Jit M, Leung KS, Zheng YM, Feng LZ, Wang LP, et al. The economic burden of influenza-associated outpatient visits and hospitalizations in China: a retrospective survey. Infect Dis Poverty 2015;4:44. [PubMed: 26445412]

[12]. Guo R-n, Zheng H-z, Huang L-q, Zhou Y, Zhang X, Liang C-k, et al. Epidemiologic and economic burden of influenza in the outpatient setting: a prospective study in a subtropical area of China. 2012;7:e41403.

[13]. Guo R, Zheng H, Li J, Sun L, Li L, Lin J, et al. A population-based study on incidence and economic burden of influenza-like illness in south China, 2007. 2011;125:389–95.

[14]. Zhou L, Situ S, Huang T, Hu S, Wang X, Zhu X, et al. Direct medical cost of influenza-related hospitalizations among severe acute respiratory infections cases in three provinces in China. PLoS ONE 2013;8:e63788. [PubMed: 23717485]

[15]. Zhou L, Situ S, Feng Z, Atkins CY, Fung IC, Xu Z, et al. Cost-effectiveness of alternative strategies for annual influenza vaccination among children aged 6 months to 14 years in four provinces in China. PLoS ONE 2014;9:e87590. [PubMed: 24498145]

[16]. Lau JT, Ng CS, Wu AM, Ma YL, Lau MMJPo. Low coverage of influenza vaccination among Chinese children aged 12–23 months: Prevalence and associated factors. 2018;13:e0205561.

[17]. Zhou L, Su Q, Xu Z, Feng A, Jin H, Wang S, et al. Seasonal influenza vaccination coverage rate of target groups in selected cities and provinces in China by season (2009/10 to 2011/12). PLoS ONE 2013;8:e73724. [PubMed: 24040041]

[18]. Suzhou Health Commission. 2020.

[19]. Zhang T, Zhang J, Hua J, Wang D, Chen L, Ding Y, et al. Influenza-associated outpatient visits among children less than 5 years of age in eastern China, 2011–2014. BMC Infect Dis 2016;16:267. [PubMed: 27287453]

[20]. Yu J, Zhang X, Shan W, Gao J, Hua J, Tian J, et al. Influenza-Associated Hospitalization in Children Younger Than Five Years of Age in Suzhou, China, 2011–2016. Pediatr Infect Dis J 2018.

[21]. National Health and Family Planning Committee. National influenza surveillance protocol. 2010.

[22]. Wang Y, Chen L, Cheng Y, Zhou S, Pang Y, Zhang J, et al. Potential impact of B lineage mismatch on trivalent influenza vaccine effectiveness during the 2015–2016 influenza season among nursery school children in Suzhou, China. Human Vacc. Immunotherapeut. 2017:1–7.

[23]. Berger ML, Murray JF, Xu J, Pauly MJJoO, Medicine E. Alternative valuations of work loss and productivity. 2001;43:18–24.

[24]. Drummond MF, Sculpher MJ, Claxton K, Stoddart GL, Torrance GW. Methods for the economic evaluation of health care programmes. Oxford University Press; 2015.

[25]. Wang Y, Chen L, Yu J, Pang Y, Zhang J, Zhang T, et al. The effectiveness of influenza vaccination among nursery school children in China during the 2016/17 influenza season. Vaccine 2018;36:2456–61. [PubMed: 29580638]

[26]. Thompson SG, Barber JA. How should cost data in pragmatic randomised trials be analysed?. BMJ (Clin Res ed). 2000;320:1197–200.

[27]. Emukule GO, Ndegwa LK, Washington ML, Paget JW, Duque J, Chaves SS, et al. The cost of influenza-associated hospitalizations and outpatient visits in Kenya. BMC Public Health 2019;19:471. [PubMed: 32326937]

[28]. Kittikraisak W, Suntarattiwong P, Kanjanapattanakul W, Ditsungnoen D, Klungthong C, Lindblade KA, et al. Comparison of incidence and cost of influenza between healthy and high-risk children <60 months old in Thailand, 2011–2015. PLoS ONE 2018;13:e0197207. [PubMed: 29771945]

[29]. Putri W, Muscatello DJ, Stockwell MS, Newall AT. Economic burden of seasonal influenza in the United States. Vaccine. 2018;36:3960–6. [PubMed: 29801998]

[30]. Esposito S, Cantarutti L, Molteni CG, Daleno C, Scala A, Tagliabue C, et al. Clinical manifestations and socio-economic impact of influenza among healthy children in the community. 2011;62:379–87.

[31]. Suzhou Statistic Bureau. Suzhou City Economic and Social Development Statistical Year Book 2018. (in Chinese). Suzhou Statistic Bureau Suzhou City Economic and Social Development Statistical Year Book 2018 (in Chinese).

[32]. Guo S, Liang X, Zuo S. Economical Burden on Measles, Rubbella, and Mumps'Cases in China in 2004. Chinese J Vacc Immunizat 2008;14:32–6.

[33]. Zhang W, Gao J, Chen L, Tian J, Biggerstaff M, Zhou S, et al. Estimated influenza illnesses and hospitalizations averted by influenza vaccination among children aged 6–59 months in Suzhou, China, 2011/12 to 2015/16 influenza seasons. Vaccine 2020.

[34]. Zheng Y, Rodewald L, Yang J, Qin Y, Pang M, Feng L, et al. The landscape of vaccines in China: history, classification, supply, and price. BMC Infect Dis 2018;18:502. [PubMed: 30286735]

[36]. Thomas RE. Is influenza-like illness a useful concept and an appropriate test of influenza vaccine effectiveness?. Vaccine 2014;32:2143–9. [PubMed: 24582634]

Table 1

Characteristics of respondents for cost-per-episode of influenza outcome estimation among children < 5-year-old in Suzhou, 2011/12 to 2016/17 influenza seasons.

	Non-medically attended [b] (n = 2,171) n (%)	**Outpatient (n = 799) n (%)**	**Hospitalization (n = 436) n (%)**
Male	1135 (52.3)	466 (58.3)	272 (62.4)
Age distribution (Month)			
0–5	–	39 (4.9)	61 (14.0)
6–23	406 (18.7)	313 (39.2)	191 (43.8)
24–35	201 (9.3)	174 (21.8)	60 (13.8)
36–59	1564 (72.0)	273 (34.2)	124 (28.4)
Household registered in Suzhou (Suzhou Hukou)	957 (44.1)	509 (63.7)	314 (72.0)
Comorbidity [a]	30 (1.4)	32 (4.0)	38 (8.7)
Hospitalized Day, median days (IQR)	–	–	7 (6,8)
Lost productivity days of caregivers, median days (IQR)	–	0 (0,2)	7 (6,9)
Lost school day, median days (IQR)	–	0 (0,2)	7 (6,9)

Data were n(%) or as otherwise indicated. IQR: Inter-quartile range.

[a] Comorbidity includes congenital heart disease, asthma and other chronic lung disease, neuromuscular disease, kidney disease, blood dyspraxia and HIV.

[b] Non-medically attended influenza was not laboratory confirmed and used non-medically attended influenza-like illness (ILI) as proxy. We assumed that the characteristics were similar between influenza and non-influenza non-medically attended ILI cases.

Table 2

Mean cost-per-episode of influenza illnesses by characteristics among children <5-year-old in Suzhou, China, 2011/12 to 2016/17 influenza seasons.

	Non-medically attended		Outpatient						Hospitalization					
	Total[c]	p	Direct[d]	p	Indirect[e]	p	Total	p	Direct[d]	p	Indirect[e]	p	Total	p
Overall Medical	9.92 (13.26)		102.56 (151.97)		58.49 (62.38)		161.05 (176.98)		1110.99 (452.34)		314.99 (272.31)		1425.95 (603.59)	
Non-medical	-		47.90 (54.81)		-		-		1000.89 (419.20)		-		-	
	-		33.37 (133.68)		-		-		110.11 (148.59)		-		-	
Age groups (month)		0.390		0.002		0.898		0.041		0.108		0.908		0.336
0–5	-		65.40 (45.04)		50.21 (25.23)		115.61 (61.61)		995.41 (377.19)		315.55 (214.83)		1310.95 (521.96)	
6–23	9.65 (21.37)		94.19 (126.77)		62.02 (77.88)		156.21 (162.20)		1125.49 (500.62)		313.16 (253.83)		1438.64 (646.99)	
24–35	8.29 (7.95)		107.00 (192.44)		54.91 (46.58)		161.91 (214.09)		1069.64 (340.98)		299.99 (241.11)		1369.63 (490.67)	
36–59	10.20 (10.83)		114.63 (158.25)		57.91 (54.37)		172.54 (177.70)		1165.53 (447.83)		324.79 (334.82)		1490.32 (617.17)	
Suzhou Hukou[a]		0.103		<0.001		0.063		<0.001		<0.001		0.096		0.202
Yes	9.68 (13.00)		112.44 (173.98)		60.59 (64.40)		173.02 (198.88)		1092.16 (406.48)		298.74 (230.10)		1390.91 (538.45)	
No	10.06 (13.41)		85.22 (100.43)		54.82 (58.58)		140.04 (127.56)		1159.45 (552.17)		356.80 (356.61)		1516.25 (740.50)	
Comorbidity[b]		0.009		<0.001		0.519		0.319		<0.001		0.750		0.969
Yes	13.95 (15.98)		106.96 (67.96)		51.63 (37.73)		158.59 (100.57)		1131.73 (453.44)		296.31 (206.76)		1428.04 (603.29)	
No	9.74 (13.10)		102.37 (154.50)		58.78 (63.20)		161.15 (179.50)		1109.01 (452.76)		316.77 (277.90)		1425.78 (604.37)	
Seasons		<0.001		<0.001		<0.001		<0.001		<0.001		<0.001		<0.001
2011/12	-		92.72 (70.85)		60.28 (71.50)		153.00 (115.06)		1055.80 (810.99)		206.51 (125.16)		1262.31 (929.60)	
2012/13	-		114.31 (95.02)		54.28 (33.20)		168.59 (121.75)		915.81 (300.83)		225.36 (137.06)		1138.16 (365.50)	

	Non-medically attended		Outpatient						Hospitalization					
	Total[c]	p	Direct[d]	p	Indirect[e]	p	Total	p	Direct[d]	p	Indirect[e]	p	Total	p
2013/14	-		69.77 (54.27)		51.98 (40.41)		118.59 (83.11)		1067.90 (293.50)		224.34 (116.77)		1292.23 (315.90)	
2014/15	11.28 (15.40)		60.92 (41.20)		45.70 (19.74)		106.61 (55.66)		1226.70 (590.83)		461.95 (345.91)		1688.66 (768.91)	
2015/16	9.45 (10.73)		278.13 (475.55)		64.70 (53.14)		342.83 (496.99)		1360.22 (529.33)		383.87 (206.64)		1744.09 (673.66)	
2016/17	5.88 (5.12)		94.47 (71.10)		75.50 (40.65)		169.97 (107.44)		1192.44 (388.58)		340.11 (359.88)		1532.55 (575.68)	

Costs per episode are in 2017 US dollars.

Data are Mean (standard deviation, SD). The means (SDs) were estimated by bootstrap resampling with 10,000 replications.

[a]Hukou: permanent household registration.

[b]Comorbidity includes congenital heart disease, asthma and other chronic lung disease, neuromuscular disease, kidney disease, blood dyspraxia and HIV.

[c]Total cost of non-medically attended influenza only includes direct medical costs.

[d]Direct cost includes direct medical cost (medicine, diagnostics, therapeutics, supplies/rooms, and services/nursing) and direct non-medical cost (transportation, caregivers lodging and nutrition supplementation attributed to the influenza illness).

[e]Indirect cost was calculated as the estimated total days of lost work due to caring for the sick child multiplied by the value of a lost time based on the human capital (Supplemental Table 1).

Table 3

Influenza ilness incidence rates and number of outcomes among children < 5-year-old in Suzhou, China, 2011/12 to 2016/17 influenza seasons.

	Incidence rate, per 100 person-years (95% CI)	Number of outcomes per year (95% CI)
Non-medically attended	1.67 (1.66,1.69)	4919 (4864,4975)
0–5 *m*	2.10 (2.03,2.17)	580 (561,599)
6–23 *m*	1.56 (1.53,1.60)	1412 (1382,1442)
24–35 *m*	2.04 (2.00,2.09)	1255 (1227,1283)
36–59 *m*	1.45 (1.42,1.48)	1661 (1628,1693)
Outpatient	7.49 (7.45,7.53)	21994 (21880,22108)
0–5 *m*	3.98 (3.89,4.08)	1101 (1075,1127)
6 –23 *m*	9.61 (9.53,9.68)	8673 (8602,8744)
24–35 *m*	7.93 (7.84,8.02)	4867 (4813,4920)
36–59 *m*	6.44 (6.38,6.50)	7365 (7298,7431)
Hospitalization	0.90 (0.88,0.91)	2633 (2592,2674)
0–5 *m*	1.76 (1.70,1.83)	487 (469,504)
6–23 *m*	1.12 (1.09,1.15)	1011 (986,1036)
24–35 *m*	0.65 (0.62,0.67)	398 (382,414)
36–59 *m*	0.65 (0.63,0.67)	742 (720,764)

CI: Confidence interval.

Table 4

Annual economic burden of influenza illnesses among children < 5-year-old in Suzhou, China, 2011/12 to 2016/17 influenza seasons.

	0–5 *m*		6–23 *m*		24–35 *m*		36–59 *m*		Total	
	Mean	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**
Total Economic burden	0.191	(0.679,0.853)	2.823	(2.57,3.077)	1.344	(1.136,1.551)	2.394	(2.155,2.632)	7.346	(6.923,7.768)
Non-medically attended [a]	–	–	0.014	(0.011,0.017)	0.010	(0.009,0.012)	0.017	(0.016,0.018)	0.049	(0.046,0.052)
Influenza outpatient	0.127	(0.105,0.149)	1.355	(1.198,1.511)	0.788	(0.632,0.944)	1.271	(1.115,1.427)	3.542	(3.272,3.812)
Lost productivity day of caregivers (median,IQR)	1101	(1101,2202)	8673	(8673,26019)	4867	(4867,14601)	7365	(7365,22095)	21,994	(21994,65982)
Lost school day (median,IQR)	1101	(1101,2202)	8673	(8673,26019)	4867	(4867,14601)	7365	(7365,22095)	21,994	(21994,65982)
Direct cost [b]	0.072	(0.063,0.088)	0.817	(0.695,0.939)	0.521	(0.381,0.661)	0.844	(0.694,0.983)	2.256	(2.024,2.488)
Medical cost	0.035	(0.025,0.044)	0.364	(0.331,0.398)	0.253	(0.222,0.284)	0.401	(0.363,0.372)	1.054	(0.993,1.114)
Non-medical cost	0.021	(0.014,0.029)	0.257	(0.170,0.345)	0.179	(0.042,0.315)	0.276	(0.150,0.402)	0.734	(0.530,0.938)
Indirect cost [c]	0.055	(0.046,0.064)	0.538	(0.463,0.613)	0.267	(0.233,0.301)	0.427	(0.379,0.474)	1.287	(1.191,1.382)
Influenza hospitalization	0.639	(0.573,0.704)	1.454	(1.361,1.549)	0.545	(0.495,0.596)	1.106	(1.024,1.187)	3.755	(3.605,3.904)
Lost productivity day of caregivers (median,IQR)	3896	(2922,4383)	7077	(6066,9099)	2786	(2090,3184)	5194	(4452,5936)	18,431	(15798,23697)
Lost school day (median,IQR)	3409	(2922,4383)	7077	(6066,8088)	2786	(1990,3184)	5936	(4452,10388)	18,431	(15798,23697)
Direct cost [b]	0.485	(0.438,0.532)	1.138	(1.066,1.210)	0.426	(0.391,0.461)	0.865	(0.806,0.924)	2.925	(2.813,3.037)
Medical cost	0.438	(0.394,0.482)	1.018	(0.948,1.087)	0.381	(0.349,0.412)	0.789	(0.738,0.839)	2.635	(2.531,2.739)
Non-medical cost	0.047	(0.031,0.062)	0.120	(0.097,0.143)	0.045	(0.032,0.058)	0.076	(0.056,0.096)	0.290	(0.253,0.327)
Indirect cost [c]	0.154	(0.127,0.180)	0.317	(0.280,0.353)	0.119	(0.095,0.144)	0.241	(0.197,0.285)	0.829	(0.762,0.897)

Annual Economic Burden is presented in millions of 2017 US dollars (95% confidence intervals).

Mean cost and 95% confidence intervals (95% CI) were estimated using bootstrap resampling with 10,000 replications.

[a] Total cost of non-medically attended influenza only includes direct medical costs.

[b] Direct cost includes direct medical cost (medicine, diagnostics, therapeutics, supplies/rooms, and services/nursing) and direct non-medical cost (transportation, caregivers lodging and nutrition supplementation attributed to the influenza illness).

[c] Indirect cost was calculated by the estimated total days of lost work due to taking care of sick child multiplied by value of a lost time based on the human capital.