Optimal age groups to target for influenza vaccination to reduce the impact of influenza in Hong Kong: abridged secondary publication

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KEY MESSAGES

1. Based on the fitted directed graph model, the probabilities of infection among household members of vaccinated and unvaccinated children were similar, suggesting limited indirect protection for household members through vaccination of children.
2. Influenza vaccination strategies targeting the age group with the highest attack rate are most effective. Children have the highest attack rate; therefore, influenza vaccination strategies targeting children can decrease the attack rate in older adults.
3. Influenza vaccination strategies targeting children are more efficient in most influenza seasons. However, attack rate and infection severity in older adults should also be considered.

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Introduction

Influenza viruses cause considerable morbidity and mortality each year. Vaccination against influenza is the most effective measure to control its spread. Influenza vaccination strategies typically target high-risk populations such as children aged <2 years, older people aged ≥65 years, individuals with chronic diseases, and pregnant women. However, mathematical models suggest that vaccination strategies targeting children are optimal in certain transmission scenarios. Vaccination as a household-level intervention can indirectly protect other family members. In Hong Kong, the risk of infection for unvaccinated members of a household with one vaccinated child was reduced by only 5%, despite a direct vaccine efficacy of 70% during the 2010 influenza B epidemic.[1]

This study aimed to explore age-specific strategies for family-level interventions (to reduce the risk of infection in unvaccinated family members) and population-level interventions (to reduce the risk of infection in non-target age groups).

Methods

Participants were recruited from two community-based randomised controlled trials to evaluate the direct and indirect benefits of influenza vaccination.[2,3] In the subsequent observational follow-up from late 2010 to late 2013, serum specimens were collected from all participants each autumn (October to December) and from 25% of participants each spring (April to May).[4] Sera were tested against influenza A(H1N1)pdm09 and A(H3N2)-like viruses for each study year, using haemagglutination inhibition assays.[1] Syndromic surveillance data in Hong Kong were used to identify influenza epidemics.

Our previous directed graph model, which estimated the probability of infection from both community and household transmission during the epidemic, was able to overcome the difficulty of using serological data with only final infection status for each participant, given unobserved transmission chains.[1,5] Two scenarios were simulated to estimate the degree of indirect protection provided by influenza vaccination. First, one child in each household was vaccinated. Second, all children in each household were vaccinated. We simulated 10 000 epidemics for each scenario with 150 000 households. In each simulation, we constructed corresponding digraphs to identify the source of each infection and estimate the probability of infection from both the community and households. The indirect protection of a vaccine strategy was estimated by the ratio of the probability of infection in a group to the corresponding probability of infection under a no-vaccination strategy.

To model vaccine strategies targeting different age groups, we used an age-structured susceptible-exposed-infected-recovered model. The model was stratified according to age group (0-17, 18-49, 50-64, and ≥65 years) and vaccination status. We then estimated model parameters using the attack rates from three influenza epidemics between 2009 and 2013. The following strategies were tested: baseline coverage, increasing coverage by 20% or 40% in the age group of ≥65 years (older adults), increasing coverage by 20% or 40% in the age group of 0 to 17 years (children), and increasing coverage by 20% or 40% in both age groups. Population size and vaccine coverage were extracted from the literature. We investigated the indirect protection provided to other age groups by vaccinating the high-transmissibility age group (0-17 years). Effectiveness was estimated by comparing the cumulative incidences of infections under different vaccine strategies with the incidence under baseline coverage.

Results

Ten rounds of sera were collected between 2009 and 2013 during six major influenza A epidemics, including a pH1N1 outbreak in 2009, two pH1N1 epidemics in 2011 and 2013, and three H3N2 epidemics in 2010, 2012, and 2013 (Fig 1).

Overall, we recruited 829 households across two trials; 86 households participated in both trials. Finally, 2512 participants were included during the pH1N1 pandemic outbreak, and 1443 to 1943 participants were included in each of the other five epidemics, after exclusion of households without complete infection status for all members.

Based on the fitted directed graph model, two strategies were simulated: vaccinating one child in each household and vaccinating all children in the household (Fig 2). In the optimal scenario, where the direct vaccine efficacy was 70%, the probability of household infection for unvaccinated adult contacts was almost halved under both strategies, compared with no vaccination. Relative probabilities ranged from 0.62 to 0.68 and 0.44 to 0.54, respectively, across the six epidemics. However, the reduction in total probability of infection was marginal because the community was the main source of infection. These relative probabilities ranged from 0.93 to 0.96 and 0.91 to 0.94, respectively.

The degree of indirect protection from vaccinating children depended on the attack rate (Table). Assuming vaccine efficacy was 60% and vaccine coverage increased by 40%, in an influenza season with a high attack rate (season 1), the attack rates for children and older adults could be reduced by 31% and 48%, respectively. When targeting only children, the attack rates for children and older adults could be reduced by 50% and 39%, respectively. These findings suggest that indirect protection from increasing vaccine coverage is greater in children than in older adults. When increasing coverage of both children and older adults by 20%, the attack rates could be further reduced by 38% and 43%, respectively. Compared with allocating all vaccines to children (coverage increased by 40%), concurrently allocating vaccines to both children and older adults (coverage increased by 20% for both age groups) reduced the attack rates by 12% less in children and 4% more in older adults. Similar patterns were observed in simulations for season 4 or when only coverage of the targeted group was increased by 20%. During season 3, the attack rate remained highest in children, but the difference in attack rates between children and older adults was smaller (0.07). Therefore, targeting children or targeting older adults brings similar indirect protection to other age groups.

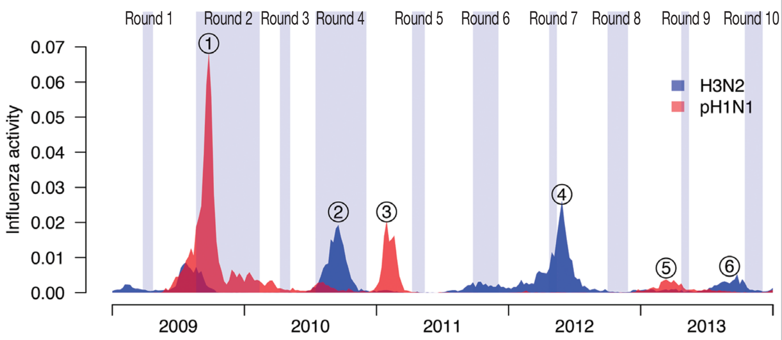

FIG 1. Influenza activity from 2009 to 2013, including six epidemic seasons and 10 rounds of sera collection.

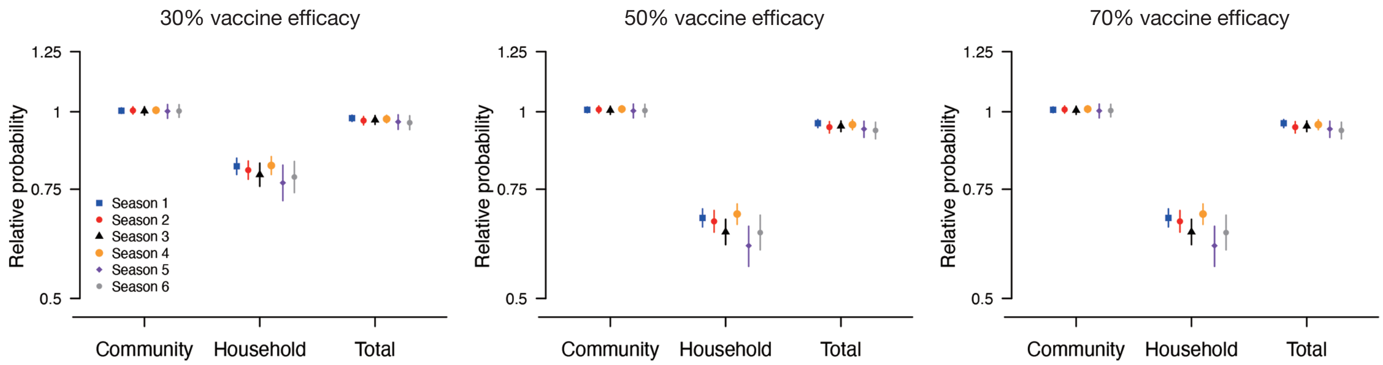

FIG 2. Relative infection probabilities (from the community, infected household members, or both) during the six epidemic seasons for household contacts of vaccinated children when all children in the household are vaccinated (strategy 2), compared with no vaccination of children. Results are shown for assumed vaccine efficacies of 30%, 50%, and 70%.

TABLE. Estimated attack rates across five influenza seasons (season 5 cannot be calibrated owing to 0 observed attack rate in older adults) under various vaccine strategies when vaccine efficacy is set to be 60%.

Strategy	Attack rate				Vaccine efficacy, %			
	Age group 0-17 y (children)	Age group 18-50 y	Age group 51-64 y	Age group ≥65 y (older adults)	Age group 0-17 y (children)	Age group 18-50 y	Age group 51-64 y	Age group ≥65 y (older adults)
Season 1 (high attack rate)								
Baseline coverage	0.403	0.115	0.066	0.205				
Increase coverage by 20% in age group ≥65 y	0.349	0.096	0.055	0.151	13	17	17	26
Increase coverage by 40% in age group ≥65 y	0.278	0.078	0.045	0.107	31	32	32	48
Increase coverage by 20% in age group 0-17 y	0.293	0.089	0.051	0.162	27	23	23	21
Increase coverage by 40% in age group 0-17 y	0.202	0.067	0.038	0.125	50	42	42	39
Increase coverage by 20% in age groups 0-17 y and ≥65 y	0.248	0.072	0.041	0.117	38	37	38	43
Increase coverage by 40% in age groups 0-17 y and ≥65 y	0.138	0.043	0.024	0.062	66	63	64	70
Season 2 (high attack rate)								
Baseline coverage	0.099	0.101	0.098	0.316				
Increase coverage by 20% in age group ≥65 y	0.067	0.068	0.066	0.199	32	33	33	37
Increase coverage by 40% in age group ≥65 y	0.044	0.044	0.043	0.115	56	56	56	64
Increase coverage by 20% in age group 0-17 y	0.082	0.095	0.092	0.300	17	6	6	5
Increase coverage by 40% in age group 0-17 y	0.066	0.089	0.086	0.285	33	12	12	10
Increase coverage by 20% in age groups 0-17 y and ≥65 y	0.055	0.063	0.062	0.187	44	38	37	41
Increase coverage by 40% in age groups 0-17 y and ≥65 y	0.029	0.038	0.037	0.101	71	62	62	68
Season 3 (high attack rate)								
Baseline coverage	0.159	0.136	0.120	0.088				
Increase coverage by 20% in age group ≥65 y	0.143	0.122	0.107	0.068	10	10	11	23
Increase coverage by 40% in age group ≥65 y	0.129	0.109	0.095	0.051	19	20	21	42
Increase coverage by 20% in age group 0-17 y	0.126	0.120	0.106	0.078	21	12	12	11
Increase coverage by 40% in age group 0-17 y	0.098	0.106	0.093	0.068	38	22	23	23
Increase coverage by 20% in age groups 0-17 y and ≥65 y	0.113	0.108	0.095	0.059	29	21	21	33
Increase coverage by 40% in age groups 0-17 y and ≥65 y	0.079	0.084	0.074	0.039	50	38	38	56
Season 4 (high attack rate)								
Baseline coverage	0.273	0.232	0.270	0.084				
Increase coverage by 20% in age group ≥65 y	0.260	0.220	0.256	0.068	5	5	5	19
Increase coverage by 40% in age group ≥65 y	0.247	0.208	0.244	0.054	10	10	10	36
Increase coverage by 20% in age group 0-17 y	0.217	0.207	0.242	0.074	21	11	10	12
Increase coverage by 40% in age group 0-17 y	0.169	0.183	0.216	0.065	38	21	20	23
Increase coverage by 20% in age groups 0-17 y and ≥65 y	0.207	0.196	0.23	0.060	24	16	15	29
Increase coverage by 40% in age groups 0-17 y and ≥65 y	0.152	0.163	0.193	0.042	44	30	29	50
Season 6 (high attack rate)								
Baseline coverage	0.077	0.057	0.093	0.091				
Increase coverage by 20% in age group ≥65 y	0.067	0.048	0.08	0.061	13	16	14	33
Increase coverage by 40% in age group ≥65 y	0.058	0.041	0.069	0.045	25	28	26	51
Increase coverage by 20% in age group 0-17 y	0.063	0.052	0.086	0.075	18	9	8	18
Increase coverage by 40% in age group 0-17 y	0.052	0.048	0.079	0.069	32	16	15	24
Increase coverage by 20% in age groups 0-17 y and ≥65 y	0.055	0.044	0.074	0.056	29	23	20	38
Increase coverage by 40% in age groups 0-17 y and ≥65 y	0.040	0.035	0.058	0.039	48	39	38	57

In influenza seasons where attack rates were comparable between older adults and children, or the attack rate in older adults was higher (eg, season 6), the attack rates in children and older adults could be reduced by 25% and 51%, respectively, if increasing vaccine coverage for older adults by 40%. When targeting only children, the attack rates in children and older adults could be reduced by 32% and 24%, respectively. In such scenarios, increasing vaccine coverage in older adults (rather than children) would be more beneficial.

Discussion

We studied the transmission dynamics of influenza A virus within households during six epidemics from 2009 to 2013 in Hong Kong to identify factors that influence transmission. We then assessed the indirect benefits of vaccinating children in households, based on different levels of vaccine efficacy. Although vaccination reduced the probability of transmission within households, its impact on the overall probability of infection for household contacts was small. Similar to our previous study on influenza B epidemics,[1] household transmission was estimated to represent approximately 10% of all transmission events during the six influenza A epidemics—lower than the 30% previously reported. This proportion could be due to higher rates of community transmission in Hong Kong, potentially because of crowded public transport and schools. Vaccine coverage in Hong Kong was low; therefore, our results should be assumed to reflect only indirect protection at the household level.

Vaccinating the age group with the highest attack rate would provide greater protection across all age groups. The attack rate was highest in children during most influenza seasons. Therefore, targeting children could provide indirect protection in most seasons, regardless of whether vaccine coverage is increased in children or older adults. Our results support implementing a transmission-limiting strategy in Hong Kong: targeting children was more effective because it could reduce the attack rate in children and thus indirectly reduce the attack rate and mortality in older adults.

However, when deciding which age group to target for vaccination, the mortality rate in older adults should also be considered. For example, when an influenza variant is associated with increased severity among older adults, vaccination of this group may remain a priority. Similarly, if a variant is more likely to infect older adults, the targeted age group should be shifted accordingly. Therefore, attack and mortality rates in older adults should be closely monitored to determine whether a modified vaccination strategy is warranted.

To estimate household transmission dynamics, we relied on a ≥4-fold rise in antibody titre to identify influenza virus infections, which may have resulted in measurement error. Our model did not explicitly include contact rates among age groups; therefore, it may have underestimated the impact of vaccine strategies targeting children.

Conclusion

Targeting children may not provide indirect protection to other household members. Individual vaccination remains crucial for protection against influenza at the household level. At the population level, targeting children is likely to be the optimal strategy because the attack rate is highest in children during most seasons. However, the severity of circulating strains in older adults should also be considered. Close monitoring of attack rates across age groups is essential to determine which age group should be prioritised for increased vaccine coverage.

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Disclosure

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1. Tsang TK, Wang C, Fang VJ, et al. Indirect protection from vaccinating children against influenza A virus infection in households. Viruses 2022;14:2097.

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