Clinical effectiveness of seasonal influenza vaccination against pandemic and seasonal influenza

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Background

Vaccination is effective in preventing infection and illness associated with seasonal influenza viruses when circulating strains match the vaccine strains.

Methods

We conducted a double-blind randomised trial in 431 individuals belonging to 119 Hong Kong Chinese households. Follow up began in November 2008 and ended in October 2009. One child aged 6 to 15 from each household was randomised to receive one dose of inactivated trivalent seasonal influenza vaccine (TIV) or saline placebo. Sera were collected from vaccinees and all household members before and after vaccination and after the winter and summer peaks of influenza activity in Hong Kong, the summer peak being succeeded by the outbreak of pandemic A/H1N1. Influenza A and B infections were confirmed by serum haemagglutination inhibition and viral neutralisation titers as well as reverse transcription polymerase chain reaction assay on nasal and throat swabs collected during illness episodes.

Results

TIV recipients had lower rates of serologically confirmed seasonal A/H1N1 infection (TIV 8%, placebo: 21%; p=0.10) and A/H3N2 infection (7% vs 12%; p=0.49), but higher rates of serologically-confirmed pandemic A/H1N1 infection (32% vs 17%; p=0.09). Household contacts in TIV group aged ≤15y had lower rate of seasonal influenza A/H1N1 (15% vs 42%; p=0.02) but non-statistically significant higher rate of pandemic influenza (34% vs 27%; p=0.72). In multivariable analysis, individuals who were infected with seasonal influenza A during the study period had a lower risk of laboratory-confirmed pandemic A/H1N1 infection (adjusted odds ratio=0.38; 95% CI: 0.16-0.92), and receipt of seasonal TIV was unassociated with risk of pandemic A/H1N1 infection (adjusted OR=1.16; 95% CI: 0.50-2.72).

Discussion

Vaccination against seasonal influenza protected against strain-matched infection in children. Naturally acquired seasonal influenza infection appeared to confer cross-protection against pandemic influenza. Whether prior seasonal influenza vaccination predisposes to a higher risk of infection with the pandemic strain requires further investigation.

Serological studies and the transmission dynamics of influenza

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Background

During and between pandemics, good knowledge of the transmission dynamics of influenza can help to improve public health decisions. Many sources of data and tools to analyse those data are available. Although a number of genuine insights were achieved using other sources and mathematical models, the absence of good serological data generated substantial uncertainty about likely epidemic trajectories.

Methods

We conducted a paired serological survey of a largely representative cohort of households in Hong Kong and gathered data on severe confirmed cases from the whole population. We also constructed a parsimonious mathematical model of pandemic influenza. We obtained values for key parameters of the model using data from the serological survey.

Results

The epidemic in Hong Kong infected many more children than it did adults. The rate of infection of older adults was low but the infection in those individuals was more severe. The skewed age distribution of infections caused a "core-group" effect resulting in a low overall infection attack rate.

Discussion

Predicting the peak of an outbreak of a novel pathogen is difficult without accurate knowledge of the rate of infections in different transmission groups. Surveillance of currently circulating strains of influenza should focus on older individuals so as to detect any antigenic evolution that renders the pandemic strain more infectious to older adults.

Exploratory research in infectious disease epidemiology – the HIV example

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HIV/AIDS is a relatively young condition, the discovery of which could be traced back to 1980 when some homosexual men were diagnosed with a syndrome characterised by profound immune deficiency. The subsequent 3 decades have witnessed epidemiology assuming a central role in HIV research, with progress made in footsteps relatively different from other prevalent infections. In profiling HIV epidemiology studies, 3 characteristics could be identified, which are becoming key learning points in epidemiology. Firstly, cohort studies have assumed an important position in describing epidemiology, as exemplified by the Multicentre AIDS Cohort Study (MACS). There are now more than 200 HIV/AIDS cohorts globally, which continue to generate new knowledge which informs clinical and public health interventions. Secondly, public health surveillance has become an expanded concept in epidemiology. The concept covers not just clinical HIV disease but infection and behaviours, which has since been named "second generation surveillance". More recently, there was the introduction of "third generation surveillance" that incorporates related morbidity/mortality data, and the monitoring of public health responses, e.g. coverage of treatment. Thirdly, methodological exploration was practised, which has led to the widespread use of molecular approaches, spatial studies, social network analysis, in advancing our understanding of the transmission dynamics of the virus and its determinants at individual, social and population levels. Illustrated by examples in Hong Kong and globally, the hallmarks of HIV epidemiology are the pursuance of exploratory research, system-building, integration of multiple approaches, and the emphasis on careful observation and community participation in the development of the analyses.

Cost-effectiveness of HPV vaccination

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Cervical cancer causes significant morbidity and mortality among women worldwide. Infection of human papillomavirus (HPV) in the cervix is the cause of cervical cancer. In addition to cervical screening which aims at early detection, vaccines which prevent infection of the two most prevalent HPV types (16 and 18) have recently been developed and are now commercially available in Hong Kong. We built mathematical models to perform cost-effectiveness analysis (CEA) to evaluate the public health impact of large-scale HPV vaccination. Moreover, we conducted surveys to investigate females' knowledge and receptiveness of HPV vaccination. In the questionnaire surveys, we interviewed 2,254 adolescent girls and 1,023 women who had daughters under 18. Thirty-three percents of adolescent girls and 45% of women would consider vaccinating themselves and their daughters, respectively. Age of vaccination was the main factor influencing tendency to vaccinate. Both groups expressed that the suitable age of vaccination was 15-16 years-old, which was older than that recommended by vaccine manufacturers (9-12 years-old). In the CEA, we developed a dynamic transmission model to estimate the herd effect of large-scale HPV vaccination. We then applied the estimated post-vaccination HPV infection rates in an individual-based model to simulate its long-term impact on cervical cancer prevention. Compared with the current screening scheme, including HPV vaccination costs USD150,000, 94,000 and 77,000 per life-year after vaccination has begun for 20, 40 and 60 years respectively. Our results suggested that adding a long-term HPV vaccination programme to current screening practice would be cost-effective in reducing the burden of cervical cancer in Hong Kong.

Exhaled air dispersion during application of common respiratory therapies

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Influenza A/H5N1 has become the major emerging infectious disease of global concern following the SARS epidemic in 2003. Respiratory failure is the major complication in patients hospitalised with influenza A/H5N1 infection, and many patients progress rapidly to acute respiratory distress syndrome and multi-organ failure with a fatality rate about 60%, which is much higher than the mortality of 10% due to SARS in 2003.[1,2]

Viral pneumonia such as SARS and influenza may potentially spread by airborne transmission. A case control study involving 124 medical wards in 26 hospitals in Guangzhou and Hong Kong has identified 6 independent risk factors of super-spreading nosocomial outbreaks of SARS: minimum distance between beds <1m, performance of resuscitation, staff working while experience symptoms, SARS patients requiring oxygen therapy or non-invasive positive pressure ventilation (NPPV) whereas availability of washing or changing facilities for staff was a protective factor.[3] Using laser smoke visualisation techniques,[4] it is noted that substantial exposure to exhaled air occurs within 0.4m and 0.8m of patients receiving oxygen via a simple mask and treatment via a jet nebuliser respectively.[5,6] NPPV via the ResMed Mirage mask may disperse exhaled air to 0.5m[4] whereas exhaled air plume increases to 0.85m from patients receiving NPPV via the Respironics ComfortFull 2 mask at predictable directions.[7] Image 3 mask, which requires connection to the whisper swivel exhalation device for prevention of carbon dioxide re-breathing, leads to more diffuse room leakage >0.95m even at low IPAP and should be avoided in patients with respiratory failure of unknown aetiology requiring NPPV.[7]

Substantial exposure to exhaled air occurs within 1m toward the end of the bed from patients receiving oxygen via nasal cannula at a larger isolation room at PMH with more efficient air exchange whereas diffused room contamination occurs at the smaller isolation room at PWH with less efficient air exchange.[8] Healthcare workers should take extra infection control precaution when managing patients with pneumonia and respiratory failure at small isolation room settings.

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Modelling infectious diseases from an engineering perspective

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Background

Generation, transport, exposure or removal of droplets and droplet residuals due to exhalation or medical procedures are governed by physical principles. Engineering control measures such as use of air cleaning and ventilation also play a part in infection control, along with administrative measures, engineering measures and use of personal protective equipments (PPE). Advanced engineering measurement and modelling methods have enabled us to understand some engineering questions in disease transmission and control, thanks to the support of RFCID.

Knowledge gained

Respiratory droplets can be anything between 0.1 and 1000 microns in diameter and the commonest diameter lay between 35 and 100 microns. Droplets larger than 60 microns are involved in large droplet transmission of diseases. Expelled droplets were carried more than 6 m away by exhaled air at a velocity of 50 m/s (sneezing), more than 2 m at a velocity of 10 m/s (coughing) and less than 1 m at a velocity of 1 m/s (breathing). Droplet residues maintain a larger size in humid air than that in dry air. The droplet residue size at relative humidity = 90% could be 1.6 times that in dry air. Large droplets are removed by deposition, and fine droplet nuclei are removed by ventilation. Human movement can promote air mixing in a ward, but this is not a crucial factor. Ventilation rate is an important parameter, and natural ventilation is now accepted by WHO for infection control when properly designed.

Impact on policies & practice attributable to infectious disease and health services research in Hong Kong

Our results showed the importance of ventilation rate in isolation rooms. The current CDC ventilation design is inadequate and a lot less effective than our newly proposed system. There may be a need to consider the proximity and short-range airborne transmission in infection control.