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Factors associated with uptake of influenza vaccine in people aged 50 to 64 years in Hong Kong: A case-control study

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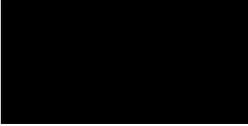


Infogr.am of the study result

The words represent factors (variables) included in the case-control study. The word sizes reflect the magnitudes of the adjusted odds ratio between cases and controls. Only some of the variables were statistically significant.

Declaration

I, Pui Shan YEUNG, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.


Sign: _____

Full name: Pui Shan YEUNG

Date: 14 October 2014

Abstract

Seasonal influenza is a serious public health problem that can cause severe illness, hospitalisation and death. Influenza vaccination is one of the most effective methods for preventing influenza and its complications. In Hong Kong, people aged 50 to 64 were added as a recommended priority target group for influenza vaccination by the Department of Health starting from 2011/12. The coverage rate of the influenza vaccine for this age group was 8.5 percent in 2012/13.

In order to explore the reasons for the low influenza vaccine coverage rate, a systematic literature review and a case-control study were conducted. The literature review aimed to explore what demographic, social and psychological factors were associated with the uptake of influenza vaccination among adults from 18 to 64 years. The result of the review was used to inform the design of a case-control study, which aimed to determine factors associated with the uptake of influenza vaccination amongst adults aged 50 to 64 years in Hong Kong. The literature review and the case-control study are presented in publication format.

The case-control study was conducted using street intercept interviews from 17 July to 15 August 2013. Cases were adults aged 50 to 64 years who received influenza vaccination in 2011/12 or 2012/13, while controls were the same as cases, except they did not receive the vaccine during the same period. Multinomial logistic regression analysis was performed on the data to explore associations between vaccination status and the variables. The study had a total of 604 respondents: 193 cases (vaccinated) and 411 controls (non-vaccinated), with a case-to-control ratio of 1:2.1. The factors which possessed the strongest associations with influenza vaccination were: 'eligible for free government vaccine'; 'willing to receive flu vaccination for free'; 'perceived having severe or moderately symptoms when contracting flu'; and 'accept advice from health professional'.

Word counts 300

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Abbreviations

ACI	Advisory Committee on Immunisation, Hong Kong, China
ACIP	Advisory Committee on Immunization Practices, US
AED	Accident and Emergency Department
CDC	Centers for Disease Control and Prevention, US
CHP	Centre for Health Protection, Hong Kong, China
CI	Confidence interval
CSSA	Comprehensive Social Security Assistance
DH	Department of Health, Hong Kong, China
DrPH	Doctor of Public Health
EBPHP	Evidence-based public health practice (a teaching module)
ECDC	European Centre for Disease Control and Prevention
EThOS	Electronic Theses Online Service
GVP	Government Vaccination Programme, Hong Kong, China
ICU	Intensive care unit
IIV	Inactivated influenza vaccines
IIV3	Trivalent live attenuated influenza vaccines
IIV4	Quadrivalent live attenuated influenza vaccines
ILI	Influenza-like illness
I-MOVE	Influenza Monitoring Vaccine Effectiveness
LAIV	Live attenuated influenza vaccines
LMD	Leadership, management and development (a teaching module)
NGO	Non-governmental organisation
OPA	Organisational and Policy Analysis
OR	Odds ratio
SARS	Severe acute respiratory syndrome
SCVPD	Scientific Committee on Vaccine Preventable Diseases
US	United States
VO	Vaccination Office, Centre for Health Protection, Hong Kong
WHO	World Health Organization

1. Introduction

1.1 Seasonal influenza vaccination for people aged 50 to 64

Seasonal influenza vaccination (referred to as vaccine or vaccination below) policy and programmes remain an important aspect of national health provision. In a World Health Organization (WHO) survey, 50% of the surveyed countries reported having established policies on seasonal influenza vaccination, and an additional 19% reported having recommendations in place for risk groups.¹ Most countries recommended that people with a high-risk of influenza-related complications or hospitalization, and people at the two extremities of age, to get vaccinated.¹

Many health authorities in the world have not provided national influenza vaccination services for people aged 50 to 64 years, with the exception of Belgium and Ireland.^{2,3} Besides, a few countries, such as the US, Austria and Estonia, recommend that all people aged 6 months or above should receive influenza vaccination.^{4,5} In Hong Kong, experts specialized in influenza vaccination have held a different view and opined that people aged 50 to 64 years should be one of the recommended group. Those who receive financial assistance in this age group were included in the Government Vaccination Programme (GVP) for free influenza vaccine since November 2011; a year after the 2009 H1N1 influenza pandemic period ended in August 2010.⁶

The Southeast Asia region, where Hong Kong is situated, is regarded as an epicentre for the emergence of new strains of human and avian influenza viruses.^{7,8} Hong Kong is the place where H5N1 avian influenza first made its appearance in 1997, and was amongst the earliest places affected by severe acute respiratory syndrome (SARS) in 2003. Additionally, it was also where the 1968 influenza pandemic (Hong Kong flu) originated. The Department of Health (DH) in Hong Kong has implemented stringent health measures against influenza and respiratory diseases.

The coverage rate for people aged 50 to 64 was very low following the launch of the new vaccination policy – just 8.5% in 2012/13⁹ and 3.1% of those eligible for

free influenza vaccine under GVP.¹⁰ There are many unsolved questions to be explored regarding the reason for this low coverage rate. This thesis begins by exploring the related demographic, social and psychological factors of vaccination behaviour.

1.2 Roadmap of influenza vaccination policy change

Influenza vaccination is constantly advancing and new discoveries have emerged as a result of continuous viral mutation, the use of new vaccines (e.g., quadrivalent influenza vaccine) and changes in the vaccine market. The revision of vaccination policy and services is an on-going task for health authorities wishing to maximize their preparedness for influenza epidemics and pandemics. The WHO advocates for countries to include recommended priority groups for annual influenza vaccination, and most countries follow their recommendations.¹¹ In the 25 countries and areas of the Western Pacific region, health-care workers and the elderly were most frequently recommended for vaccination; 96% countries and areas recommended vaccinating these groups, followed by pregnant women (76%), people with chronic illnesses (72%) and children (60%).¹

Take the example of the US to illustrate the evolution of the influenza vaccine policy on recommended groups. Over the last three decades, the Advisory Committee on Immunization Practices (ACIP) has made a number of stepwise incremental changes to the annual influenza vaccine recommendations. Finally, in 2010 its recommendation included all of the US population aged 6 months and older.^{12,13} From the 1960s to 1986, the categories of persons recommended for influenza vaccination in the US were primarily those who were at high risk from complications, such as the elderly, persons with chronic medical diseases, pregnant women, and children.¹² These groups are the same as those recommended by the WHO today.¹¹

Since 1987, ACIP expanded vaccination to include people in contact with high-risk individuals; i.e., home carers and caregivers of high-risk groups were recommended.¹⁴ From 2000 to 2009, the ACIP has incrementally added more and more subgroups to its recommendations: in 2000, adults from 50 to 64;¹⁵ in 2004, children aged 6 to 23 months;¹⁶ in 2006, children aged 24 to 59 months; in 2008, children aged 5 to 18 years;¹⁷ and in 2010, national universal recommendations for all persons 6 months and older.¹³

If policy in the US represents the movement towards a universal recommendation for vaccination, then many other developed countries are situated at various stages along this path. In 2009, the US was the country with the largest influenza vaccine dose distributed anywhere in the world.¹⁸ Europe and the Americas account for 75% to 80% of the global influenza supply each year.¹⁸ In a study of 29 European Union (EU)/European Economic Area (EEA) countries, the ‘WHO-recommended high-risk groups’ were all or partly accepted by all countries; household contacts with high-risk groups were recommended by half of the countries.¹⁹ A minority of European countries (Austria, Belgium, Estonia, and Ireland) was ahead and included those aged 50-64 in their recommended groups, although this recommended group does not necessarily receive reimbursement for vaccination.²⁰

Ideally, public health policy should be founded on an evidence-based decision making process. Scholars have agreed that this complicated process requires an integration of evidence from multiple domains across disciplines.²¹ Concerning the influenza vaccine policy change, at least three areas have to be considered, namely: 1) the best available research evidence on vaccine efficacy and effectiveness, disease burden, economic evaluation, and vaccine safety; 2) practitioner expertise and other available resources, including prioritisation of health needs, availability of skilled staff, and vaccine transport/logistic/storage/disposal; and 3) the perception, values, affordability, and preferences of people and stakeholders.^{22,23} In the real world, policy change is not always backed up by solid scientific evidence. Even in the US, an authoritative review report has criticised ACIP’s recommendations as ‘often...[being] based on professional judgment and not on scientifically sound data’.¹² This might have been more the case in the past when data was not easily accessible, as well as in resource-limited developing areas.

In Hong Kong, immunisation against various infectious diseases has been implemented since the 1960s.²⁴ In 1992, an Advisory Committee on Immunisation (ACI) was set up under the DH to review strategy on immunisation.²⁵ Since 1998, the Government has been providing free seasonal influenza vaccination to target groups at public hospitals/clinics. In 2004 after SARS, the Scientific Committee

on Vaccine Preventable Diseases (SCVPD) was set up to succeed ACI. The SCVPD has included all the 'WHO-recommended high-risk groups'. Later, it expanded its recommended group to include children aged 6 months to 5 years in 2008/09, and those aged 50 to 64 years in 2011/12.^{6,26} It is an exciting prospect to follow up on the effectiveness of these vaccination implementations in Hong Kong and explore how they are contributing to controlling influenza outbreaks.

1.3 Influenza vaccination policy changes in Hong Kong

1.3.1. Rationale and evidence-based drivers behind policy change

The major driver behind the vaccine policy change in 2011/12 was due to a real increase in influenza-attributed ICU admissions and deaths among the 50 to 64 years,⁶ plus an anticipated increase in the years to come when the influenza A(H1N1)pdm09 strain was predicted to circulate in the population. This group was more susceptible than the other recommended groups to severe influenza complications in the 2011/12 winter.⁶ The offer of vaccine was the best method for protecting against influenza-related hospitalisation.

Although there can be other direct and indirect benefits resulting from the expansion of the vaccine-recommended group, these were not stressed in the health policy documents. Such benefits could include a decrease in work-day loss and an in-direct protection of household vulnerable groups by herd immunity (elders and children). There was no noted advocacy by healthcare providers - inside or out-side the government - to push the change of this policy.

A number of enabling factors facilitated this policy decision and its implementation. A well-established annual seasonal vaccine delivery system in the public and private clinics, and hospitals, was already in place; and with more than 150 vaccination locations.²⁷ There was flexibility for policy makers to decide whom to include for free or subsidised vaccination so as to control the costs incurred. Plenty of vaccines were supplied by at least 5 vaccine companies at steady market prices.²⁸ A preliminary enquiry of healthcare providers and medical associations indicated that they seemed to have welcomed the change. Although there was a concern that once the recommended group was expanded, it would not be easy subsequently to remove this group from the list. Besides, previous local study did not support the cost-effectiveness of the influenza vaccine for the working-age population and the elderly.²⁹

1.3.2. Expected public health impact and outcomes

The expected impact following the implementation of the influenza vaccination programme to include the 50 to 64 years age group would be a decrease in severe influenza complications. This outcome would be monitored by regular hospital

surveillance on the number of ICU admissions and deaths. There was also an expected increase in vaccine coverage for this age group. DH did not set a target on the coverage, partly because there was no vaccine coverage data collected for this age group at that time. A surrogate marker as pre-policy coverage was that 13.1% of adults in Hong Kong received an influenza vaccine within the past 12 months.³⁰ There would be an expected indirect cost reduction in terms of work production and decreased infection of household members due to herd immunity.²⁹

1.3.3. Process of policy change

In early January 2011, the surveillance system in the Department of Health (DH) documented an increase in the number of hospital admissions due to influenza among people aged 15 to 64 years.³¹ As a result, a new surveillance mechanism was set up on 24 January 2011 to monitor the situation. Since then, public and private hospitals have had to report all influenza-associated deaths and admissions to intensive care units (ICU) to the DH during peak influenza seasons.³¹

In April 2011, a Working Group on Influenza Vaccination under the DH studied the local epidemiology and possible causes of the increase in hospitalisations. The group concluded there was a real increase in ICU admission and fatal influenza cases in healthy individuals aged 50 to 64 years in the winter of 2010/11. The incidence of ICU admission or fatal influenza cases was 1.8 per 100,000 people in those aged 50 to 64 years.³² This incidence was higher than the corresponding numbers in any other age group, including young children aged below 6 years (0.7 per 100,000) and elders over 65 (0.6 per 100,000).⁶ In addition, most (41%) of the influenza-related deaths had affected people aged 50 to 64 years. In contrast, during previous influenza seasons – excepting summer 2009 – about 85% of all fatal cases of influenza occurred in the elderly over 65 years old.³²

In May 2011 the Working Group presented the findings to an expert panel – the Scientific Committee on Vaccine Preventable Diseases (SCVPD) – to review influenza vaccination policy for the following year.⁶ In June 2011, the SCVPD suggested expanding the recommended priority groups to include people aged 50 to 64 years in 2011/12.³² The decision was based on the local context, the

likelihood that the influenza A(H1N1)pdm09 strain would continue to circulate in the coming years, and that the vaccine had good protection against clinical influenza in healthy adults.⁶

DH had studied and advised the Government on the health needs, the cost and feasibility of providing free or subsidized influenza vaccinations to this additional target group, for inclusion in the 2011/12 Government Vaccination Programme* (GVP). Based on the DH and SCVPD's recommendations, the Government approved extending the scope of the free vaccination in the 2011/12 GVP, launched on 1 November 2011, to cover recipients of the Comprehensive Social Security Assistance (CSSA)[†] aged 50 to 64.^{33,34} No free or subsidized influenza vaccination service was provided by Government to non-recipients of CSSA.

Table 1 Timeline on events of the policy change

Dates (2011)	Events
Early January	Observed an increase in the number of hospital admissions due to influenza among people aged 15 to 64 years
24 January	Set up a new surveillance mechanism in all public hospitals
April	Working Group on Influenza Vaccination reviewed the situation
May	SCVPD reviewed influenza and the vaccination policy
July	SCVPD advised DH on expanding the recommended priority groups to include people aged 50 to 64 years in 2011/12
July to September	DH studied and advised the Government on the extension of GVP to cover recipients of the CSSA aged 50 to 64
1 November	Launch of 2011/12 GVP

1.3.4. Low influenza vaccination coverage (the problem)

The coverage rate for people aged 50 to 64 was very low following the launch of the new vaccination policy on the 1 November 2011. In 2012/13, only 8.5% of all people aged 50 to 64 received influenza vaccination⁹; while in 2011/12, 3.1% of eligible people in this age group were administered free influenza vaccine under the Government Vaccination Programme.¹⁰ By comparison, vaccination coverage

* Under the GVP, free seasonal influenza vaccination is provided to eligible persons at public clinics.

[†] CSSA Scheme is a social safety net for those who cannot support themselves financially. It is designed to bring their income up to a prescribed level to meet their basic needs.

in 2012/13 for children under 5 years, elders over 65 years, and people with chronic diseases were 28.4%, 39.1% and 28.2%, respectively.⁹ The figures show that vaccination coverage was low, in those who were eligible for free vaccination and those who paid out-of-pocket.

1.4 Thesis overview

1.4.1. Research aim

The overall research aim of this thesis is to explore the reasons for the low influenza vaccine coverage rate (8.5% in 2012/13) in people aged 50 to 64 in Hong Kong.

1.4.2. Research objectives

1. To assess the health needs for influenza vaccination in people aged 50 to 64 in Hong Kong using epidemiological, comparative and corporate approaches.
2. To examine factors associated with the uptake of seasonal influenza vaccination in adults aged 18 to 64 years old by systematic literature review.
3. To determine which factors (variables) were associated with influenza vaccine uptake in residents of Hong Kong aged 50 to 64 years in 2011/12 and 2012/13 using a case-control study.

1.4.3. Knowledge gap

Why another study on influenza vaccine uptake?

Since healthy middle-aged adults have not previously had been the focus of efforts to promote influenza vaccination in many countries, a review of the literature yielded only a few publications on their vaccination behaviours.^{35,36} Besides, these studies used national data collected a decade ago. There has been one Hong Kong survey published as ‘Letter to the Editor’ in 2013 by Prof Shui Shan LEE, who is a member of my Advisory Committee for this research³⁷, which stated that the vulnerability of people 50 to 64 year for influenza ‘is less well appreciated’ compared to elders.

This research also quantifies the association between the factors associated with the uptake of influenza vaccine more precisely with regard to the 50 to 64 age group. It recruited a sufficient number of cases (vaccinated respondents) so that even a small OR of 2 could be detected at a significance level of 0.05 and power level of 80%. The sample size of this age band is larger than vaccination surveys with thousands of subjects targeted to explore issues pertinent to the whole Hong Kong population.^{9,38} The result is that this study provides related new data and understanding of vaccination behaviour in this age group, and will serve as a

reference for health workers planning influenza vaccination services and devising health promotion strategies.

1.5 Thesis structure

This Doctor of Public Health (DrPH) thesis is a hybrid of traditional and publication formats. The document provides a complete and systematic account of the research, presented in a logical and connected manner. Two research papers prepared for publication have been included in chapters 3 and 5, respectively.

Chapter 1 introduces the thesis. Chapters 2 to 5 then address the three research objectives listed above in Section 1.3.2. The methods and results of each research questions are presented within these chapters.

Chapter 2 provides background information on the local context, i.e., the needs of influenza vaccination for people aged 50 to 64 in Hong Kong. It presents the epidemiology, diseases burden, control measures, cost-effectiveness, vaccination policy, and stakeholders' perspectives on influenza vaccination for this age group.

Chapter 3 is a research paper based on a systematic literature review of the factors associated with the uptake of seasonal influenza vaccination in adults aged 18 to 64 year-old.

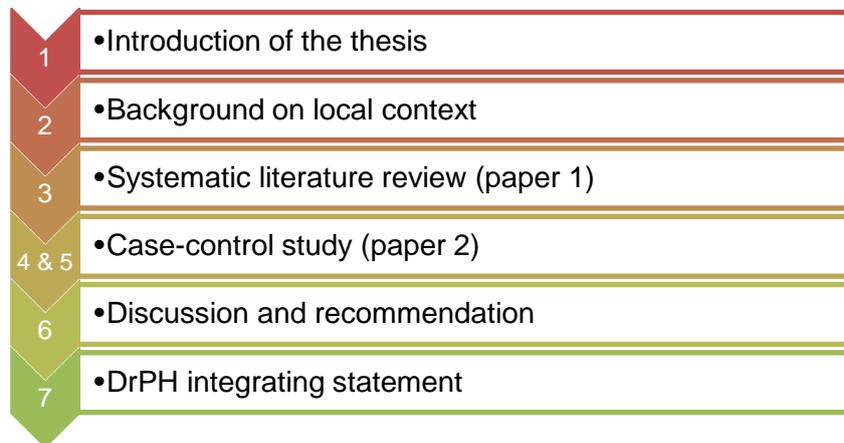
Chapter 4 contains information on the design and pilot of the case-control study to determine factors associated with the uptake of seasonal influenza vaccine in people aged 50 to 64 years in Hong Kong.

Chapter 5 is a research paper on the case-control study. The unpublished subgroup analysis of the research results is also included.

Chapter 6 presents an overview of the thesis as a whole, and contains a discussion of the results of all the chapters. It also points out the implications of the findings on health service and policy, suggests potential areas for future research, and details the dissemination plan of the research findings.

Chapter 7 is an integrating statement summarising the learning processes over the course of the DrPH degree. It is followed by the annexes as supplementary information, and references.

Figure 1 DrPH thesis structure



1.6 Role of the researcher

Being a public health physician in the DH Vaccination Office, I was an officer accountable to the government influenza vaccination programmes from 2009 to 2012. From 2010 to 2012, I was a member of the team which was responsible for assessment, formulation, promotion, execution, and evaluation of the expansion of influenza vaccination service for people aged 50 to 64.

I proposed this research because I was dissatisfied with the extremely low vaccination coverage in the above age group after the Government Vaccination Programme was launched. I generated the research framework and methods; drafted research protocols and questionnaires; identified, analysed and interpreted the data; and finally wrote and revised the report. The data collection was assisted by interviewers from a marketing company. I personally analysed the data and consulted a statistician on statistical formula, statistical analysis and interpretation. The thesis has been copy-edited by Mr. Cathel Hutchison to ensure a high standard of language and structure.

1.7 Timeline

I commenced the research in May 2012. Planning and preparation for the case-control study took a year to undertake, before the pilot was conducted in June 2013. I collected the data in July and August of 2013. My research time line is shown in the Gantt Chart in Table 2.

Table 2 Gantt Chart showing the research timeline

Task	Start	Finish	Duration (Month 2012 - 2014)																											
			2012												2013												2014			
			5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	
Supervision and monitoring																														
1 Meeting with supervisor	Cont'	-																												
2 Seek advisory committee members' advice	Cont'	-																												
3 Send progress report to advisory committee	Cont'	-																												
4 Meeting with advisory committee	Cont'	-																												
Review meeting																														
1 Prepare review report	May 12	May 13																												
2 Prepare DrPH review meeting	Aug 12	Nov 13																												
3 Prepare resubmit review report	Nov 12	Jun 13																												
Ethics approval																														
1 Prepare / renew ethical approval (local)	Aug 12	May 13																												
2 Prepare / renew ethical approval (LSHTM)	Sep 12	Jul 13																												
Systematic literature review																														
1 Conduct database search, review and writing	Mar 13	Aug 13																												
2 Revise, update and rewrite search	Nov 13	Mar 14																												
Case-control study																														
1 Pilot survey	Jun 13	Jun 13																												
2 Data collection	Jul 13	Aug 13																												
3 Data input and collation	Jul 13	Sep 13																												
4 Data validation and quality control	Aug 13	Sep 13																												
5 Data entry and cleaning in database	Aug 13	Oct 13																												
6 Analyse data	Oct 13	Jan 14																												
Writing-up																														
1 Prepare first draft of the thesis report	Sep 13	Apr 14																												
2 Finish first draft on two published articles	-	15/3/14																												
3 Revise thesis report	Apr 14	May 14																												
4 Submit thesis report	15/5/14	n/a																												
Examination																														
1 Prepare for exam	May 14	Jul 14																												
2 Viva	15/7/14	-																												

2. Background on health needs

This chapter uses epidemiological, comparative and corporate approaches to provide background information on the local context, i.e., the need for influenza vaccination amongst people aged 50 to 64 in Hong Kong. The needs assessment draws upon the models of Stevens and Gilam³⁹ and Wright and Cave.⁴⁰ Table 3 summarises the framework of this needs assessment, as well as the approaches, tasks, information used, and the sources drawn upon.

In brief, an epidemiological approach explores what is effective and for whom.³⁹ Using this approach, local surveillance data was collected to identify and quantify the epidemiological nature of influenza. The cost-effectiveness of vaccination and the current service were then reviewed.

A comparative approach is then employed to compare the levels of service provided to different populations.⁴⁰ Following this, an examination of influenza vaccination recommendations, service provisions and cost-effectiveness analyses of vaccination programmes for the 50 to 64 population in other countries has been conducted. To do this, information was gathered from health authorities' publications and cost-effectiveness studies.

A corporate approach is used to explore stakeholders' demands, wishes and alternative perspectives on the influenza vaccination service. Stakeholders in this study included experts, policy-makers and users. Their views were collected through meetings, surveys, published literatures, and communication of different forms.

Table 3 Approach, task, information and sources for the needs assessment

Approach	Task	Information on	Source of information
Epidemiological (chapter 2.1)	To identify the health problem	Local influenza epidemiology (2.1.1)	<ul style="list-style-type: none"> • Surveillance data from DH and WHO
	To estimate the size and nature of the problem	Disease burden of influenza, vaccine coverage and health status (2.1.2)	<ul style="list-style-type: none"> • Local surveillance data from hospitals • Vaccination statistics from DH
	To study the mode of transmission	Influenza transmission (2.1.3)	<ul style="list-style-type: none"> • Published literature from medical databases
	To explore influenza vaccine as an intervention to reduce	Vaccine effectiveness, efficacy as an methods to reduce influenza transmission (2.1.4)	<ul style="list-style-type: none"> • Published literature from medical databases
	To review existing vaccination services	Current local service provision (2.1.5)	<ul style="list-style-type: none"> • Programme data and budgets from DH and online information
Comparative (chapter 2.2)	To compare overseas influenza vaccination recommendations and services	Health Authorities' recommendation on influenza vaccination (2.2.1)	<ul style="list-style-type: none"> • National health authorities documents • WHO website
		Experience of national vaccination service (2.2.2)	<ul style="list-style-type: none"> • Reports from health authorities
		Disease burden of ILI (2.2.3)	<ul style="list-style-type: none"> • Published literature from medical databases
		Health economic evaluation on vaccination (2.2.4)	<ul style="list-style-type: none"> • Published literature from medical databases
Corporate (chapter 2.3)	To find out what experts, professionals and user want	Experts', professionals' and stakeholders' opinion and view (2.3.1)	<ul style="list-style-type: none"> • Scientific Committee expert opinion • Meetings with health-care providers
		Users' attitude, knowledge, perception and behaviour (2.3.2)	<ul style="list-style-type: none"> • Studies and surveys on patient opinion • Published literature from medical databases

2.1 Epidemiological Approach

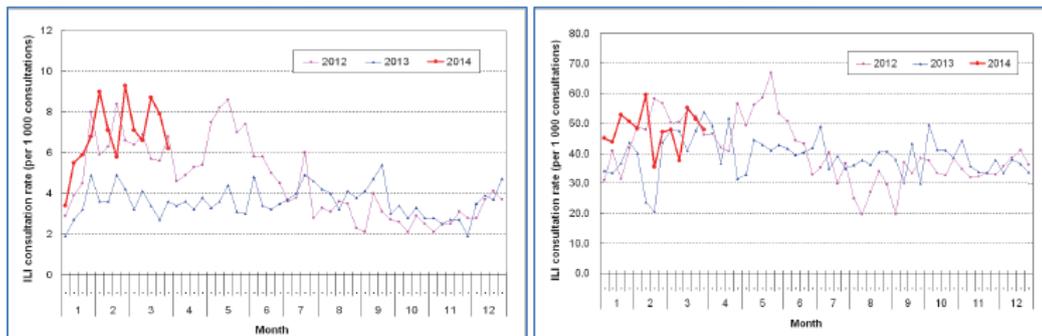
2.1.1. Local influenza epidemiology

Hong Kong is a high-density city with population of 7.18 million people living in 1,104 km².⁴¹ People aged 50 to 64 constitute 22% of the population or 1.56 million, with more than 95% of them being Chinese.^{41,60} The city is located on the coast of Southern China and has a subtropical climate. The Southeast Asia region is regarded as an epicentre for the emergence of new strains of human and avian influenza viruses.^{7,8}

In Hong Kong, seasonal influenza is usually more prevalent from January to March and July to August, as reflected by the epidemiology surveillance data from the sentinel surveillance system, hospitals and laboratory.^{6,42} For the past three years, the average influenza-like illness (ILI) consultation rate among general outpatient clinics ranged from 1.9 to 9.3 per 1000 consultations, and among sentinel private doctors ranged from 20 to 60 per 1000 consultations.⁴³ (Figure 2 & 3)

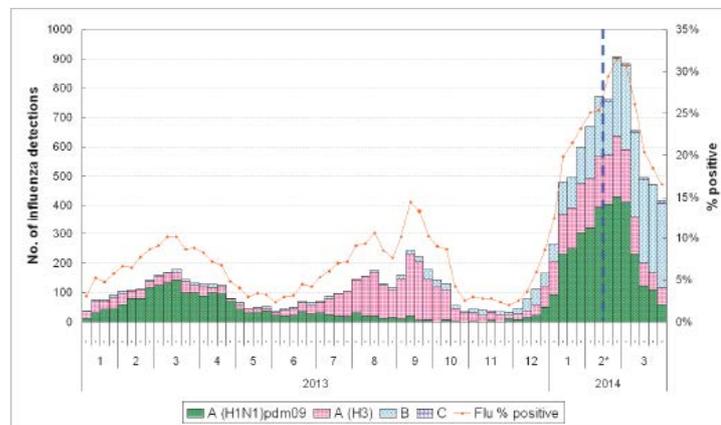
There is a ten-fold ILI consultation rates difference between general outpatient clinics and private doctors was mainly due to disease case mix. Study showed among patients had upper respiratory tract infection, 19% consulted the general outpatient clinics and 81.3% consulted private doctors.⁴⁴ Recent study showed doubled the attending patients identified general outpatient clinics as their main provider for chronic disease management than private doctor.⁴⁵ The difference in patient demography should have also contributed but this is harder to quantify.

Figure 2 & 3 Influenza-like illness surveillance among sentinel general outpatient clinics (left) and sentinel private doctors (right), 2012-2014⁴³



From 2009 to 2011, influenza A(H1N1)pdm09 was the predominant influenza strain in Hong Kong.⁴⁶ In 2012, influenza A(H3N2) (48.4%) and influenza A(H1N1)pdm09 (47.4%) were the major circulating viruses.⁴⁷ In the winter of 2013/14, influenza A(H1N1)pdm09 predominated (72%) while in 2013 summer it was influenza A(H3N2) (85%) (Figure 4).⁴³ Similarly, these two influenza viruses have been the predominant viruses in 2013 and early 2014 in Southeast Asia and China.^{48,49} So far, the majority of influenza A(H1N1)pdm09 tested in other parts of the world and in Hong Kong remains sensitive to oseltamivir and there has been no observed trend in increasing oseltamivir-resistance.^{49,50,51}

Figure 4 Influenza virus detections in 2013-14⁴³



2.1.2. Estimate size and nature of the problem

Worldwide disease burden of influenza

Every year, influenza epidemics result in substantial morbidity, mortality and economic loss: 250,000 to 500,000 deaths worldwide, 3 to 5 million cases of severe illness, and 2% to 10% annual attack rate with 0.6 to 2.5 workdays lost per illness.^{52, 53, 54} The estimated rates of influenza-associated deaths varied substantially by age group in different seasonal influenza epidemics, but were usually highest amongst elders.

Influenza in working adults results in substantial health-care demand, direct medical costs, and indirect costs from work absenteeism and reduced productivity induced by the illness. No estimated figure was found in Hong Kong. The US Centers for Disease Control and Prevention (CDC) estimated that 2 to 10% annual attack rates result in 0.6 to 2.5 workdays lost per illness.^{52,53,54}

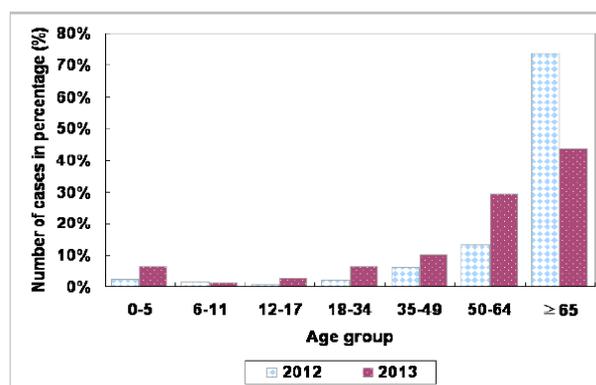
Local disease burden of influenza

In Hong Kong, the modelled estimated of deaths from seasonal influenza was 7.3 deaths per 100,000 population per year for those aged 40 to 65 years, and 102.0 deaths for those aged above 65.⁵⁵ These figures for Hong Kong were similar to those for the US, which were estimated as 7.5 and 98.3 per 100,000 population per year for those aged 50 to 64 and ≥ 65 respectively.⁵⁶

According to the local hospital record of fatal cases who had been diagnosed as having influenza in public hospitals from 2005 to 2011, the number of influenza-related deaths mainly affected persons aged 65 or above and children in the past influenza seasons.³² Only after the 2009 pandemic, the age group 50 to 59 was more affected. The deaths of these cases were mostly due to influenza A(H1N1)pdm09.⁵⁸ From 2000 to 2010, the median annual hospitalization rate of influenza A was consistently higher than influenza B for all age groups.⁵⁷

In 2013, Hong Kong had the usual bimodal influenza pattern with a winter peak (January to May 2013) and a summer peak (July to October 2013).⁵⁸ In the winter peak, there were 78 ICU admissions, including 29 deaths, with laboratory-confirmed influenza infections.⁵⁸ The majority (79%) of these were infected by influenza A(H1N1)pdm09. Elders aged ≥ 65 years and those between 50 to 64 years constituted 44% and 30% of all severe cases respectively (Figure 5).⁴⁷ A high proportion (78%) of these severe cases had underlying illnesses. The total number of ICU or death cases recorded was higher in the winter than in summer. On average, around 4 ICU or death cases per week were recorded in both the winter and summer peak.⁵⁸

Figure 5 Age distribution of the severe cases in 2012 and 2013 Jan to May⁴⁷



Local vaccine coverage

Influenza vaccine coverage of all recommended priority groups ranged from 8.5% to 39.1% in 2010/11 to 2012/13.⁵⁹ In 2012/13, coverage amongst children under 5 years, elders over 65 years, and people with chronic diseases were 28.4%, 39.1% and 28.2% respectively.⁹ In the general population aged 18 or above, 14% received an influenza vaccination in the past 12 months.³⁸ In 2012/13, 8.5% of all people aged 50 to 64 received influenza vaccination.⁹

Table 4 Seasonal influenza vaccination coverage in Hong Kong 2012/13^{9,38}

Population groups	Seasonal influenza vaccination coverage (%)
Children aged 6 months to 5 years	28.4
Persons aged 18 or above	14
Persons aged 50 to 64 years	8.5
Persons aged 65 years or above	39.1
Persons with chronic medical problems	28.2

* Respondents from different age groups with self-reported chronic medical problems were counted separately in the category “Persons with chronic medical problems”.

Local health status

Persons with pre-existing chronic diseases, such as cardiovascular disease and metabolic disorder, had much higher rates of ICU or fatal outcomes across all ages for seasonal patterns. People aged 50 to 64 constitute 22% of the population or 1.56 million in Hong Kong, with more than 95% of them being Chinese.^{41,60} Hypertension is a common disease (48.4%) amongst the 55 to 64 year old population.⁶⁰ The leading cause of death for people aged 45 to 64 was malignant neoplasm (53.6%), disease of the heart (11.7%) and injury, poisoning and certain other consequences of external causes (6.6%).⁶¹

Undiagnosed or asymptomatic cardiovascular, pulmonary diseases in the local 50 to 64 aged population could be high. A local study reported only 28% of men and 30% of women in the general population with diabetes mellitus knew that they had this condition.⁶² Another study on adults aged above 20 with hypertension, showed that only about half of them (46%) were ever diagnosed as hypertensive by a doctor.⁶³

2.1.3. Influenza transmission

Reviews suggested droplet, aerosol and contact transmissions are possible routes of influenza virus transmission.^{64,65,66} The transmissibility of seasonal influenza was estimated by modelling data from the US, France and Australia over the past 30 years, with data suggesting a basic reproduction number (R_0)[‡] from 0.9 to 2.1.^{67,68} Different climate variables, such as temperature and humidity, affect the transmissibility and mode of transmission of influenza.^{69,70} The spread is also determined by people's social contact and mixing patterns, such as exposure time and degree of physical contacts.⁷¹

Experts generally agree that vaccination is the first line of defence for reducing influenza morbidity and mortality.⁷² There are other public health measures that could mitigate the spread and impact of influenza. These include: social distancing measures (isolation, quarantine, school closure); personal behavioural change (wearing masks, decrease social gathering); disinfection (hand washing, checks for fever); antiviral medication; international travel measures (travel advice, entry screening) and risk communication.⁷³

2.1.4. Immunisation to reduce influenza transmission in healthy adults aged 18 to 64 years old

Seasonal influenza vaccine protection depends on how closely matched the vaccine viruses component and the circulating viruses are, how well a person generates antibodies, and the timing of the vaccination. WHO stated that “in industrialized countries, influenza vaccines offer approximately 70–90% protection against clinical disease in healthy adults, provided there is a good match between the vaccine antigens and circulating virus(es).”^{52,74} This statement is commonly cited without detailed explanation of what it actually means. Therefore I conducted a literature search to examine how protective the influenza vaccine is for healthy adults aged 18 to 64 years old. The results are summarized below.

[‡] R_0 is the average number of secondary cases infected by each primary case

Types of influenza vaccine

Commonly available seasonal influenza vaccines can be broadly classified into inactivated influenza vaccines (IIV) and live attenuated influenza vaccines (LAIV). Inactivated influenza vaccines come in the form of trivalent vaccine (IIV3) and quadrivalent vaccine (IIV4), and they consist of three or four seasonal influenza viruses respectively. There are two different influenza type A strains and one influenza type B strain for IIV3 and an additional type B strain for IIV4. IIV3 have been used for over 60 years and IIV4 was newly registered in 2014. LAIV was registered from 2009 to 2013 for use among healthy non-pregnant people aged 2-49 years, but it is currently not registered in Hong Kong.^{26,75}

Only inactivated TIV, but not live attenuated influenza vaccine, was recommended for use by SCVPD for those aged 50-64.²⁶ In addition to the intramuscular route, an intradermal TIV for adults aged 18 years or above has been licensed in Hong Kong since December 2009. Research demonstrated that the intradermal injection resulted in similar antibody responses in people aged 18-60.⁷⁶

Indicators of vaccine protection

The serum antibody response to the haemagglutinin (HA) is most commonly used to indicate influenza vaccine efficacy. This also serves as a benchmark for licensure of IIVs. Scientists are still exploring whether hemagglutination-inhibition (HAI) antibody titre is a good indicator of vaccine protection, and in search of other serology biomarkers.^{77,78} Before a new vaccine is authorised, vaccine efficacy is evaluated in randomized controlled clinical trials conducted in healthy individuals of different age groups.⁷⁹ Following the introduction of vaccination programs, vaccine effectiveness (VE) in the community is best determined through observational studies.⁷⁹

Vaccine efficacy

A recent meta-analysis analysed eight randomised controlled trials of adults aged 18 to 65.⁸⁰ The result demonstrated the pooled efficacy of IIV3 against culture confirmed influenza to be 59% (95% CI 51%-67%). Another Cochrane review on vaccine for health adult estimated a higher vaccine efficacy of 73% (95% CI 54%-84%), when content matched WHO recommendations and circulating strain but

decreased to 44% (95% CI 23% to 59%) when it did not.⁸¹ The efficacy of LAIV was shown by several studies to be comparable with IIV.^{82,83}

Age and immune response

A quantitative review found that antibody response in the elderly (>65 years) is considerably lower than in younger adults and was estimated to be 17-53%.⁸⁴ The limited efficacy of inactivated influenza vaccine in elderly individuals is associated with decreased production of vaccine-specific antibodies, rather than a reduced quality (avidity) in antibody.⁸⁵ Since aging is a gradual physiological process, it is probable that vaccine efficacy will slowly drop when age advances for middle-age adults towards their 60s. There have been attempts by vaccine manufactures to improve the vaccine protection, such as increasing the dose of antigen, intradermal administration, adding of adjuvants, etc. Some of these new products have been authorised and marketed.⁷⁹

Vaccine effectiveness (VE)

Many countries, including the US, Europe, the UK, Canada, and Australia, conduct annual large-scale VE studies to monitor the performance of vaccine in the community. Their findings contribute to vaccine strain selection as well as for disease surveillance. A good example is the Influenza Monitoring Vaccine Effectiveness (I-MOVE) in Europe.

Review and studies on VE for IIV have shown variable results in different vaccination seasons. The VE depends very much on the degree of antigenic matching between vaccine and the circulating virus stain, and could range from negative to 70%.^{81,82} VE estimates also differ because of clinical consultation outcome measurements, the use of study methodology and residual confounding factors.^{86,87}

For example in 2012/13, nearly all the influenza A and B viruses detected globally were antigenically similar to the WHO's recommendation for the influenza trivalent vaccine.⁴⁹ The US CDC and European Centre for Disease Control and Prevention (ECDC) estimated that the interim VE against all influenza types in their target groups in 2012/13 was 62% and 50.4% respectively, both indicating a

moderate effectiveness.^{88,89} Whereas in 2011/12 when there is poor antigenic matching, the VE estimated by the I-MOVE study in Europe was 25%.⁹⁰

Reduction in workday loss and physician visit

A Cochrane review demonstrated that influenza vaccination has a modest effect in reducing influenza symptoms in healthy people aged 16 to 64 years old and on decreased the working days lost.⁹¹ In healthy adults younger than 65 years, influenza vaccination reduced ILI, working days lost and physician visits in years when the vaccine and circulating viruses were similar, as proven by randomized control trials conducted in the US in 1990s.^{92, 120} For working adults aged 50 to 64 years, research found that vaccination was associated with a significant reduction in the rate of ILI (adjusted odds ratio, 0.48; 95% CI 0.27–0.86) and fewer days of illness, absenteeism, and impaired on-the-job performance.⁹³

Pandemic influenza vaccine

High-risk group receipt of influenza A(H1N1)pdm09 monovalent vaccine was associated with and a very high reduction in infection, hospital admission and severe complications.⁹⁴ An observational study in Scotland showed monovalent influenza A(H1N1)pdm09 vaccine has a VE of 77% in preventing laboratory-confirmed influenza; and 19.5% prevention of influenza-related emergency hospital admissions.⁹⁵ In the last ‘Hong Kong Flu’ pandemic in 1968 to 1969, the monovalent vaccine VE for H3N2 was effective 65% against ILI, provided 93% protection against influenza, and 65% against hospitalisations.⁹¹

Currently, seasonal and pandemic influenza vaccines are manufactured in exactly the same manner.¹² If the manufacturing technology has not much improved since the 2009 H1N1 pandemic, there will probably be insufficient quantities of vaccine available quick enough, at least in the early phase of the next pandemic.

Safety and adverse events

The vaccine is safe and severe adverse events are rare. The most common adverse effects following IIV administration include transient local reactions (15-20%), such as pain and swelling. Some common systemic side effects are fever, headache, malaise, and myalgia. Severe adverse events such as Guillain-Barré

syndrome (1 to 2 per 1 million vaccines), meningitis or encephalopathy (1 in 3 million doses distributed), and anaphylaxis (9 in 10 million doses distributed) are rare.^{26,96,97} According to the DH Pharmacovigilance Unit, there were two serious adverse events (one Guillain-Barre Syndrome and one transverse myelitis) following seasonal influenza vaccination in 2010/11. Each severe adverse event was reviewed by DH and so far DH continues to support that this vaccine is safe.

The most common adverse reactions following LAIV administration ($\geq 10\%$) are runny nose or nasal congestion in all ages, fever $> 37.8^{\circ}\text{C}$ in children 2-6 years of age, and sore throat in adults.^{26,98}

Summary on vaccine protection

After the review and analysis, I concluded that annual vaccination remains an effective way to prevent seasonal influenza, mitigate the severity of illness and reduce the impact of the disease for adult below 65. The influenza vaccine offers good efficacy despite variations of VE in some seasons.

2.1.5. Current local service provision

Starting from 1 November 2011, people aged 50 to 64 years in Hong Kong were added as one of the nine priority recommended groups for receiving influenza vaccination.⁹⁹ Free vaccination was available to people aged 50 to 64 years receiving CSSA and those with chronic medical problems under the Government Vaccination Programme.¹⁰⁰§ Five percent of people aged 50 to 64 fell into this group.^{101,102} The remaining 95% have had to pay out-of-pocket and attend private clinics if they want to receive influenza vaccination.

Those eligible for free government vaccine may attend one of 150 public clinics for vaccination service.²⁷ Those who wanted to pay out-of-pocket can attend over 1,600 private clinics providing influenza vaccination service.¹⁰³ Public clinics and private practices are widely distributed throughout the region.

§ Those with chronic medical problems are already included in the Government vaccination programme. These are people who have chronic cardiovascular (except hypertension without complication), pulmonary, metabolic or renal problems.

The price of the vaccination should be affordable to the majority of people aged 50 to 64. The charges for one dose of influenza vaccine, including the cost of the vaccines and consultation fees, ranged from HKD\$140 to HKD\$280 (USD\$18 to USD\$36), with a median of \$180 (USD\$23).¹⁰⁴ Given the majority (~70%) of the people aged 50 to 64 earned \$4000 to \$19999 (USD\$513 to USD\$2564) a month, the price of the vaccine is 0.7-3.5% of their monthly income.⁴¹ Most of the male (89%) and female (55%) in their 50s were employed. For those aged 60 to 64 years, half of the males were still working.⁴¹ However individuals in low-income families without CSSA - e.g. housewives, unemployed and new-immigrants - are neglected and less likely to pay out-of pocket for the vaccine.

2.2 Comparative approach

2.2.1. Health Authorities' recommendation for people aged 50 to 64 years

Many developed countries recommend the influenza vaccination for children, pregnant women, elders, health-care workers, and those with chronic diseases. However, the upper age limit for influenza vaccination recommendation differs between countries. The US, Austria and Estonia recommended that all people aged 6 months or above receive influenza vaccination; and Belgium and Ireland included those aged 50 to 64 years old.^{4,19, 105, 106} WHO and some countries (Australia, Canada, Taiwan, UK) recommend those of 65 years or older.^{107, 108, 109, 110, 111} China¹¹² and several European countries (Germany, Hungary, Iceland and Greece)¹⁰⁶ recommended age 60 or above. Most countries did not include adults aged below 60 without other risk indications as their recommended group for seasonal influenza vaccination.¹¹⁰

2.2.2. Overseas national vaccination service provision

In the US, the Advisory Committee on Immunization Practices had recommended that healthy adults aged 50 to 64 be vaccinated since 2000.¹⁵ The US CDC opined that an age-based influenza criterion for vaccination, may be more successful in reaching individuals with medical conditions that put them at higher risk of influenza complications, as compared with criteria based on recognition of the specific high-risk disease conditions.¹⁵ Other benefits included decreased work absenteeism and the need for medical visits and medication, including antibiotics.¹¹³ The coverage rate of this age band in the US was 45.1% in 2012/13.¹¹⁴

In Belgium, 54% of the target group received an annual vaccination,² in contrast around 29% in Ireland.¹⁹ In Austria, influenza vaccination is recommended for everyone since 2002, including those over the age of 50 years. Only eight years later in 2010, the US recommended universal influenza vaccination. However, the influenza vaccination rate amongst the general public is low (<10%) in Austria and the number of vaccine distributed has even been in decline since 2006.²⁰ Estonia is another country which recommends influenza vaccination to 50 to 64 year olds, with a low coverage of 1% among children and the elderly.^{19,105} In both Austria and Estonia, people have to pay for the full cost of vaccination, and the

lack of free or subsidised vaccination is probably one of the key reasons for the low coverage rates.

2.2.3. Disease burden of ILI of 50 to 64 years

ILIs was common in the community, and accounted for a large portion of illness, work loss, and impaired work performance during the influenza season.¹¹⁵ For people aged 50 to 64, ILI was responsible for 45% of all days of illness during the influenza season and 39% of all illness-related work days lost.¹¹⁵ In the US study, amongst those people not under high-risk, the mean cost per case (USD\$22,304) and the medical cost per death (USD\$118,575) was highest for the 50-64 years among all the other age groups. Of the total economic burden of influenza which included all kinds of medical costs, death and loss of earning, 64% was borne by those ≥ 65 years; 50–64 years bore 21%; 18–49 years bore 10%; and children bore 5%.¹¹⁶

In the 2009 pandemic, the WHO recorded the highest case fatality rate amongst the 50-60 year-old population in many countries.¹¹⁷ The influenza A(H1N1)pdm09 strain disproportionately affected children and young adults, with the highest rate of severe disease leading to hospitalisation in those under 5 years. Reviews suggested there could possibly be partial immunity to the influenza A(H1N1)pdm09 virus in the older population.¹¹⁸ This might explain why the incidence of severe influenza complication in the elderly was relatively smaller than in those between 50-60 years.

2.2.4. Health economic evaluation on influenza vaccination

Economic analyses of influenza vaccination amongst adults aged 50 to 64 varied markedly between places. Among the economic appraisal methods, cost-effectiveness analysis (CEA) and cost-utility analysis (CUA) are commonly used as economic evaluation tools to assess influenza vaccination.¹¹⁹ Many studies have indicated that vaccination targeted at specific groups reduces health-care costs, direct medical costs and indirect costs from work absenteeism, and increases productivity.^{53,92,120} The challenge of interpreting the impact and cost-effectiveness of influenza vaccination from these studies lies in the details of the

model assumptions, such as case definition, disease burden estimates and vaccine efficacy estimation.¹²¹

Cost effectiveness studies in Australia¹⁰⁸, the UK¹²² and the US¹²³ suggest that national influenza programmes for 50 to 64 years olds were highly effective; and likely to be cost-effective in Spain¹²⁴, Brazil, France, Germany and Italy.¹²⁵ Among these countries, the cost-effectiveness ratio from the perspective of the healthcare system, ranged from US\$1,151/quality adjusted life year (QALY) saved in Brazil to US\$38,316/QALY in Italy.^{108,119-125} This is highly cost-effective if benchmarked against the UK cost-effectiveness threshold, set by the National Institute for Health and Care Excellence, of \$40,000 to \$60,000 per QALY gained.¹²⁶ There was even a net-cost saving from a societal perspective, indicating that the calculated cost incurred to vaccination programmes was less than the cost resulting from work day loss, medical care and others costs combined.^{108, 119-125}

A local Hong Kong study indicated that territory-wide influenza vaccination for the working age population did not cut publicly-funded medical costs, with an estimated cost-benefit ratio of 3.81:1^{**}.²⁹ The working age population referred to all adult, and as such, there was a substantial proportion of healthy young adults included in the model. There were also assumptions that a lower influenza-attributable hospital admission rate and a low absenteeism of workers than other places. These model assumptions lead to a low cost-effectiveness in the research result. Another study in Hong Kong found that the influenza vaccination of elderly people (aged 65 years or above) living in the community was cost-effective from a societal perspective.¹²⁷ Locally, it is possible that an influenza vaccination policy targeted towards the higher end of the age range from 50 to 64 years would be more cost-effective.

^{**} By proportion HK\$3.8 spent on vaccination can save HK\$1 because influenza-like illness has been prevented.

2.3 Corporate approach

2.3.1. Experts', professionals' and stakeholders' opinion and view

Many health authorities in the world have not provided national influenza vaccination services for the group under study, despite studies demonstrating the cost-effectiveness of this approach. Local experts specialized in influenza vaccination in Hong Kong held a different view. A meeting was convened by DH on June 2011 and the panel of experts in the SCVPD suggested including adults aged 50 to 64 years as a high-risk target group for vaccination.³² The decision was based on the local context, the likelihood that the influenza A(H1N1)pdm09 strain would continue to circulate in the coming years, and a good protection provided by the vaccine against clinical influenza in healthy adults.⁴

Internal meetings and communications with representatives of public health-care providers of DH clinics and public hospitals were held. The meetings collected views on the feasibility of expanding service provision to include giving free vaccination to eligible people aged 50 to 64. Most services agreed that they had the capacity to undertake the additional workload.

2.3.2. Users' attitude, knowledge, perception and behaviour

Determinants of health behaviours, in particular on uptake of influenza vaccination, have been extensively examined from different perspectives. In performing a systematic review of the literature in Chapter 3, numerous studies were found on attitude, knowledge, perception, and behaviour towards influenza vaccination. The literature primarily focuses on elders, children, health-care workers and other high-risk populations. Healthy middle-aged people had not previously been the focus of efforts to promote influenza vaccination in many countries. As such, only a few publications on healthy middle-aged adults were found.

Two local surveys on public's perception of influenza vaccine, which included middle-aged adults, were identified. One household survey was conducted on people aged 50 to 64 years³⁷ and the other general population survey was on adults aged 18 years and above.³⁸ The former survey found that 'previous vaccination history' and 'age between 60 to 64' were the main associations with

vaccination. The general population survey was conducted by the Hong Kong Medical Association in 2013 on adults aged 18 years and above. It found that the two most common reasons for refusing vaccination were 'in good health condition, and were not afraid of getting influenza' (39%) and 'no such habit/never thought of/not necessary' (18%).

There were also several local surveys conducted by DH¹²⁸ and local universities on public's attitude on the monovalent H1N1 vaccine.^{129,130} In these surveys, perceptions of the low risk of the pandemic influenza and concerns about adverse effects after vaccination were the primary reasons for avoiding vaccination. Respondents seldom complained about cost and accessibility.

In the US, the 2004 National Immunization Survey showed that older age (OR 1.4 to 2.1), higher education level (OR 1.4), recent doctor visit (OR 2.0), and beliefs about vaccine effectiveness (OR 2.7) were variables which were frequently positively associated with increased vaccination in people aged 50 to 64 years.³⁵ In 2003, a national Australian study on the determinants of vaccination in people aged 40 to 64 years and over, identified that the choice of influenza vaccination was influenced more by beliefs on vaccine effectiveness (OR 4.8), having medical risk factors (OR 4.8), and in occupational risk group (OR 2.4), than socio-demographic factors such as gender and income.³⁶

2.4 Discussion and Summary on needs assessment

2.4.1. Discussion

Epidemiology approach

The epidemiological approach demonstrated that influenza accounted for a substantial mortality and morbidity in people aged 50 to 64. The conclusion was mainly based on local ICU admission and fatal cases, the disease pattern of the influenza virus and the vaccination status of people aged 50 to 64. The evidence was convincing, but there were limitations to the hospital surveillance data. The admission criteria for local ICU admission in each hospital differed and it was uncertain whether physicians' had a preference for admitting patients from certain age groups. It would be useful to compare previous trends but information is not available in the public domain.

In many parts of the world, influenza A(H1N1)pdm09 disproportionately affected children and young adults, with the highest case fatality was recorded in the 50 to 60 year-old population.¹³¹ Review suggested there could possibly be partial immunity to the influenza A(H1N1)pdm09 virus in the older population.¹³² This hypothesis was supported by subsequent studies which showed 33% of humans over 60 years had cross-reacting antibodies to influenza A(H1N1)pdm09 virus by hemagglutination-inhibition and neutralization tests.^{132,133}

In 2010, WHO estimated that influenza A(H1N1)pdm09 would continue to circulate for some years to come¹³⁴, and it has continued to be the major circulating strain in Hong Kong since its emergence in 2009. The attack rate of the influenza A(H1N1)pdm09 strain is expected to decrease in subsequent years because more people have developed immunity following infection or vaccination. In addition, other strains could possibly become predominant and present a different epidemiological pattern. Local surveillance does not indicate the current dominant influenza virus H3N2 has increased serious influenza complications in people aged 50 to 64.¹³⁵

Local cost-effectiveness studies on the 50 to 64 age groups have not indicated that influenza vaccination has been cost saving from a society-wide perspective. Some reviews even doubt the effect of vaccination in reducing hospital admission and

complication rates in healthy people aged 16 to 64.^{80,170} The seasonal vaccine in 2014/15 will contain influenza A(H1N1)pdm09 component and protect the 50 to 64 age group from this virus, which has caused high ICU admission and deaths in this age group.¹³⁶

Comparative approach

Except in the US, Austria and Estonia, most countries did not include healthy adults aged 50 to 64 as a recommended target group. Similar to the US, Hong Kong had low influenza vaccine coverage and a high proportion of diagnosed chronic diseases (diabetes and cardiovascular disease) amongst adults in their mid-50s. The US strategy is to use an age-based vaccination criterion in defining risk group and covered those aged 50 to 64, regardless of their chronic disease status. This could reduce severe influenza complications and death by vaccinating all with know or unknown chronic disease status.

Based on the searched information, I could not determine why health authorities have chosen not to provide government influenza vaccination services for healthy individuals between 50 to 64 despite favourable findings in cost-effectiveness studies. Possible reasons for this could be insufficient evidence, inappropriate study assumptions, overlapping vaccination services by employers or private companies, or strained health-care manpower in the public sector. The experience in Hong Kong differed from other countries in term of health-care systems, vaccination coverage, disease patterns and acceptability of influenza vaccination. Overseas practices and recommendation from overseas studies were not directly applicable in a local setting.

Corporate approach

The local professions in the SCVPD agreed that there was a need to recommend that the 50 to 64 year-old should be offered vaccination. For the general public, surveys have informed us that many Hong Kong adults perceive vaccination to be unnecessary and worry about the side effects. The findings highlighted the discrepancies between the normative need of the professionals and the felt need of the public. Health promotion strategy should be formulated to decrease this gap and increase the acceptability of the influenza vaccination service.

2.4.2. Summary

In Hong Kong, influenza causes significant illness and economic loss among people aged 50 to 64. The vaccination rate in this age group was low (8.5%). Most countries did not include healthy adults aged 50 to 64 as a recommended target group for seasonal influenza vaccination. Local experts expressed that there was a need to vaccinate this group, but most adults in the population did not perceive this need.

3. Systematic literature review (Research paper 1)

This chapter examines what factors associated with the uptake of seasonal influenza vaccination in adults aged from 18 to 64 years old. It presents a research paper based on a systematic review of the literature, as well as related unpublished data.

3.1 Research paper 1

Title: Factors associated with the uptake of seasonal influenza vaccination in adult: A systematic review

Author(s): May PS YEUNG, Richard COKER

Type of publication: Original contribution

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Candidate's role: I conceived of the study, wrote the systematic review protocol. I reviewed all the searched titles and abstracts, and read all of the selected full text articles as an independent reviewer.

Keywords: seasonal influenza vaccine uptake, systematic review, healthy adults, associated factors

Word count abstract: 239

Abstract

Background

Seasonal influenza ('influenza') epidemics results in significant economic loss due to worker absenteeism and decreases in productivity in the general adult population. Influenza vaccination ('vaccination') has proven to be effective but vaccine coverage for non-high risk adults is low in many countries. Studies on different populations have shown a variety of factors that influence attitudes in the general population on vaccine uptake.

Objective

This study aims to use a systematic and evidence-based approach to explore the demographic, socio-psychological factors associated with the uptake of influenza vaccination amongst adults from 18 to 64 years.

Methods

A systematic literature review was performed on literature searched in databases EMBASE, MEDLINE, Cochrane Library and Electronic Theses Online Service (EThOS), up until November 2013. A critical appraisal framework was designed to assess the methodological quality of the studies.

Results

Twenty-three articles met the inclusion criteria and were selected for outcome analysis and 21 are quantitative observational studies. Advance in age and having chronic diseases were strongly indicative of vaccine uptake. Perceptions such as vaccine efficacy and vaccine safety and adverse events, were more influential than the level of knowledge on influenza and its vaccination. Advice from doctors/health professionals/family/close friends, and free vaccination, were also key factors in association with uptake of vaccination.

Conclusion

This study highlighted that perceptions, advice from doctors/health professionals/family/close friends and free vaccination were changeable factors that are positively associated with influenza vaccination in adults aged 18 to 64 years.

Introduction

Seasonal influenza ('influenza') is a constant public health threat that causes severe illness, hospitalisation and death amongst high-risk groups. Influenza transmission largely occurs in the community, and large-scale and frequent epidemics can result in significant economic losses due to worker absenteeism and decreased productivity.^{1,2} Controlling the incidence of seasonal influenza remains a challenge.

For most healthy adults, influenza is a mild and self-limiting disease. Influenza vaccination is effective in reducing influenza-like illnesses, working days lost and physician visits.^{3, 4} A recent review showed no evidence that vaccination can reduce hospital admission or complication rates.⁵

The vaccination coverage rates in non-high risk adults of 18 years and above have been low in many developed countries. Non-high risk groups usually include individuals of less than 65 years of age without a chronic disease, as well as those not working in the health-care sector. In Australia, European countries and the US, the influenza coverage rates in non-high risk adult ranged from 5.8% to 35.7%.⁶⁻⁸

In a global policy survey, 40% of the 157 countries reported having an established policy regarding seasonal influenza vaccination.⁹ The WHO and the health authorities of most countries do not recommend healthy adults to receive annual vaccination against seasonal influenza.¹⁰ Some exceptions include the US, Austria and Estonia, who recommended that all people aged 6 months or older should receive influenza vaccination.¹¹⁻¹³

The recent pandemic in 2009 may have shifted perspectives on vaccinating healthy adults. Reviews on international epidemiology reported that influenza A(H1N1)pdm09 virus disproportionately affected and increased hospitalisation and death in adults aged below 65.¹⁴⁻¹⁶ It was estimated that 80% of deaths in the pandemic 2009 were amongst people younger than 65 years of age. This differed markedly from typical seasonal influenza epidemics, during which 80-90% of deaths are estimated to occur in people of 65 years and older.¹⁷ Similarly, in the influenza pandemic in 1969/70, people of working age were most severely

affected.¹⁸ The influenza A(H1N1)pdm09 virus continued to be the predominant circulating strain in North America, Europe and China after the 2009 pandemic.¹⁹

Other benefits of vaccinating healthy adults included decreased work absenteeism and need for medical visits and medication, including antibiotics.²⁰ Besides, many middle-aged adults have undiagnosed medical conditions such as diabetes mellitus.^{21,22} Vaccination provides moderate protection to both high-risk and non-high-risk groups from influenza as well as its complications.^{5,23}

More recent reviews have found that the use of influenza vaccine was associated with a lower risk of major adverse cardiovascular events.²⁴ This may be due to physiological changes in the lungs by the influenza virus in lower blood oxygen levels, or directly injure heart muscle cells, leading to heart failure.²⁵

In many countries, only high-risk groups are subsidised or offered a free vaccination service. Health authorities have generally concentrated their vaccination promotion campaigns on high-risk groups. A better understanding of the reasons behind people's choice of vaccination will guide the planning of health and promotion programmes for improving general population vaccine coverage.

Objective and PICOS

The objective of this paper is to systematically review factors associated with the uptake of the seasonal influenza vaccination (refer as influenza vaccine or vaccine below) in healthy adults aged 18 to 64 years. Details associated with the research question formulated using population PICOS are:²⁶

- Participants: studies of adults from general population aged 18 to 64 years
- Intervention/exposure: any factors affecting the outcome, e.g., demographic, psychosocial, health-care system associated with outcome
- Comparator: those who did not receive annual seasonal influenza vaccination
- Outcome: uptake of receiving influenza vaccination
- Study design: all types of studies with quantitative data on the strength of association between intervention and outcome.

Method

A systematic review was performed in November 2013 on published literature in medical databases EMBASE (1947 to 2013 November), MEDLINE (PubMed) (January 1966 to October 2013) and Cochrane Library (1996 to present) including Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE) via Cochrane Library.

Additional search

The search was further amplified by scanning the reference lists and bibliographies of relevant papers. Search for dissertation and theses from Electronic Theses Online Service (EThOS) using the defined keywords was also performed.

Inclusion criteria

Subjects were individuals aged 18 to 64 years in the general population, irrespective of influenza immune status. The publications were in English.

Exclusion criteria

Studies were excluded if:

- more than 50% of study participants were not adults from the general population aged 18 to 64 years, e.g., health-care workers, pregnant women or patients with chronic disease(s); or only subjects from high-risk group were sampled.
- the study aim/objective was only related to the 2009 H1N1 pandemic vaccination

Keywords

Keywords used include a combination of free text terms and Medical Subject Heading (MeSH). Search terms for included seasonal influenza vaccin*, influenza vaccin*, human, accept*, attitude, intent* and perception.

Study selection and data extraction

Articles were first screened by title, then abstract and/or full text. For selected articles, the following data was extracted for each selected article: author and date of publication; place; study design; time of data collection; theoretical model used (if any); and factors associations with intentions/behaviour.

Assessment and reporting of included studies

Since most of the selected studies were observational studies and surveys, a critical appraisal framework was designed to assess the methodological quality of non-randomised trials. For these studies, the transparency or clarity of the reporting is considered key.²⁷ Reference has been made to the US CDC Transparent Reporting Evaluations with Nonrandomized Designs²⁷ and National Health Service's (NHS) Critical Appraisal Skills Programme (CASP)²⁸ in reviewing the quality of the articles. The reporting of this review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement.²⁹ This is to ensure scientific rigour and comprehensiveness in reporting.

Results

The search was performed on November 2013 and a total of 2,235 articles published in English were identified. Twenty-three articles fulfilled the inclusion criteria were retained for critical appraisal and analysis. Most of these articles are quantitative observational studies. There were eighteen cross-sectional surveys; 1 case-control study; 1 randomised-control trial; 2 longitudinal studies; and 1 meta-analysis. The studies were carried out in the following countries: Australia, China, Japan, 11 European countries, France, Netherland, Spain, and the US. The data of the articles were collected from 1997 to 2012. Twenty-one of these articles were of high or moderate methodological quality. The summary of the characteristics and key results of these articles are shown in Table 1.

The uptake of vaccination is known to be associated with multiple factors. In the selected studies, the results were mostly subjective opinions given by study participants, rather than an objective accounts using health-care quality indicators. The strengths of associated factors with influenza vaccination uptake are presented by adjusted odds ratios (ORs) in Table 2.

The associated factors were categorised into 8 groups (demography, knowledge, need, health behaviour, belief and perceptions, health-care system, advice and social support and external environment). The important findings from each article have been included. The quality of the evidence (i.e., OR) of individual factors are shown in Table 2, and this is based on critical appraisal of the cited articles.

Theories and models of behaviours

Most selected articles did not state what behavioural theory or model they used. The Health Behavioural model was the commonest model and was cited in three articles. The Protection Motivation Theory, Theory of Reasoned Action, PRECEDE model and Utilities Theory were each used separately in one article.

Demography

Increasing age was an important factor associated with uptake of vaccination in studies in European and Asian populations (OR 1.06-23.7).^{6, 31, 39, 41} Education level and being health professionals were inconsistently associated with getting vaccinated in different studies.^{6, 37, 39, 40, 48} Sex, ethnic origin, income, employment and household size were not consistent predictors of influenza vaccination in different European countries.^{6, 36}

Knowledge on influenza and influenza vaccine

There was a weak association between increased knowledge and vaccination, and the strength of association was relatively weak when compared to most of the other groups. People with better knowledge of influenza and its vaccination (OR 1.6-3.3)^{39,45} and on the effective measures to prevent influenza (OR 1.59-3.06)⁴⁵, were more likely to get vaccinated. Those who had better knowledge of vaccination required annually (OR 1.59)³⁹, vaccine being recommended to some high-risk groups (OR 1.30)⁴⁵, and on other general information of influenza transmission and treatment (OR 1.25)³⁵, were slightly more likely to choose to be vaccinated than those without adequate knowledge.

Needs

Presence of chronic disease(s) was the most frequently stated reason for people getting vaccinated (OR 1.38-13.7).^{6, 31, 32, 35-37, 40, 43, 48} Recent visits to a medical doctor may or may not be associated with vaccination.^{31, 44, 45} People consulted doctors for acute and chronic illnesses and therefore visiting a medical doctor did not imply having long-term illnesses. The association of living with children or elders at home was inconclusive.^{48, 50} It is uncertain if self-reported health status had an association.^{38, 44}

Health behaviour

Previous influenza vaccination was a good predictor for subsequent vaccination (OR 4.06-5.18).^{33, 40, 43, 50} Health behaviour such as smoking was not associated.^{42, 50} No data was found on other health behaviours such as drinking or frequent exercise.

Belief and perceptions

Belief and perception were difficult to distinguish from each other so they were grouped under the same heading. Perception of vaccine efficacy (OR 2.7-10.55) had the strongest association in this group.^{37, 44, 45} Perceived vaccine safety and adverse events after vaccination were a concern (OR 10.5) and fear of adverse reaction deterred people from getting vaccinated (OR 0.21).⁴⁵ Perceived chances of contracting influenza (OR 1.62-5.40) and perceived health impact of having influenza (OR 2.21) were also positively associated with intention to get vaccinated.³⁹ It is inconclusive whether fear of injections had an association.^{38, 45}

Health-Care System

Free vaccination (OR 4.5-7.8) was strongly associated with vaccination.^{46, 48} People who had easy access (OR 1.8) and who were satisfied with health-care service were more likely to receive the influenza vaccine (OR 1.23).^{31, 42} The usefulness of interventions to remind clients, such as telephone calls and post card reminders, was uncertain.⁴⁶

Advice and social support

Doctors' advice (OR 4.03-7.82) and health professionals' advice (OR 1.23-13.0) was significantly correlated with influenza vaccination.^{6, 31, 45, 47} Recommendation from health-care workers was an intervention encouraged by many of the selected articles based on its strong association. Relatives' or close friends' advice (OR 17.74), or they having received influenza vaccination in the last year (OR 6.44), were associated with acceptance of influenza vaccine in a Japanese study.^{45, 47}

External environment

Past experiences of infectious diseases and widespread severe epidemic could influence people's perception of vaccination.⁵² The post-pandemic effect on seasonal influenza vaccination varied in different places. In Beijing China, a study did not find impact of the 2009 pandemic on vaccination in the 2010/11 season.⁵¹ In France, there was a moderate negative effect of the 2009 pandemic on vaccination in the following two seasons.³⁰

Discussion

A person's decision to uptake influenza vaccination is influenced by a number of contributing factors. Most of the selected articles were surveys and they reflected the conscious subjective opinion of individuals. Choice of uptake could be also influenced by change of health service, media, culture, values and social norms.

Interpretation of the result

This study is a systematic and evidence-based approach to the survey design. A range of odds ratios for factors associated with influenza uptake are presented and grouped artificially into 8 domains. The studies reviewed used broad and imprecise terms, e.g. 'knowledge of influenza and influenza vaccination' or 'access to health-care settings' could be subject to individual interpretation. Hence the odds ratios are not meant to be compared by their absolute values, neither within nor across domain. However, the consistency and coherence of high ORs of a factor was strongly indicative of a high strength of association across populations.

Advance in age and having chronic disease(s) were the two most consistent and strongly associated factors with influenza vaccine uptake. Increase in age usually

increases the chance of contracting chronic diseases so these two factors were related.

Perceptions such as vaccine efficacy, and safety and adverse events, were more closely related to vaccination than knowledge. Meta-analysis supported risk perceptions are central to many health behaviours.⁵³ Although there is a general consensus that knowledge is positively correlated with positive health behaviours, the selected studies demonstrated a mild association of the two here.

If greater knowledge increased the tendency to be vaccinated, one would expect doctors, nurses and other health professionals to have a high vaccination rate, irrespective of whether it was compulsory or not. However, being a health professional was not associated with vaccination in some European countries (Germany, Italy and Poland).⁶ The coverage rates were generally low amongst health professionals in the same study on 11 European countries, with coverage ranging from the lowest at 6.4% (Poland) to 26.3% (Czech Republic).⁶ Of course, a belief in the professional duty of care or a perception of a greater occupation hazard would also provide reasons for health professionals to be vaccinated.

Advice from health professionals/family/close friends, and free vaccinations, were crucial factors which determined the choice of many to be vaccinated. Hence, health professionals could help to implement influenza vaccination programmes and contribute to increasing the vaccination coverage rates in their patients.

Past experiences of influenza pandemic vaccination and the widespread severe epidemic, could influence perception on vaccination. Although evidence demonstrated that pandemic was only insignificantly or moderately negatively associated with (i.e., reduce) later seasonal vaccination.

Excluding articles from pH1N1 vaccine

The reason for excluding articles related to the pH1N1 pandemic vaccination was the determinants for influenza vaccination were different from that of pandemic vaccination.⁴⁸ Systematic reviews found that younger age, believing in vaccine safety and/or effectiveness, and higher socioeconomic status, were important

determinants of the pH1N1 vaccine.^{54, 55} The perceived mild nature of the disease was one of the major reasons the public refused the pH1N1 vaccine.⁵⁶ The impact of extensive media publicity on Guillain-Barre syndrome and adverse pregnancy outcomes could have caused a reduction in the pH1N1 vaccination campaign worldwide. In addition, the pH1N1 vaccine was a one-off dose and administered as an emergency measure in the pre-pandemic time. Therefore, the types and magnitudes of factors associated with the uptake of vaccination could possibly differ.

Heterogeneity and unsuitability for pooling results using meta-analysis

While the selected studies all examine the factors associated with the uptake of the seasonal influenza vaccination, there are substantial heterogeneities amongst them. There is diversity in the demography of the study respondents because data was collected from more than 15 countries. Methodological variation exists because studies had different aims, sampling subject recruitment criteria, scope of question asked, and outcomes measurement.

A meta-analysis of the adjusted ORs in the selected articles was not performed. Firstly, since most of the associated factors (variables) were examined in one to three studies, pooling of data would not represent the overall result. Secondly, meta-analysis is unsuitable for a group of studies with sufficient heterogeneity. Thirdly, observational studies were conducted in non-controlled environment subject to much bias and residual confounding. Meta-analysis should be considered when a group of studies is sufficiently homogeneous in terms of participants, interventions and outcomes to provide a meaningful summary.¹³⁷

Common confounders and effect modifiers

Health seeking behaviour is a complex model and factors could possibly interact with one another. For example, advice from a doctor and health professionals could be linked to other associated factors. Older people and those with chronic disease(s), visit their doctors more frequently. The frequency of doctor visits could also be influenced by gender, ethnic origin, income, employment, household size, etc. Personal contact with a doctor and health-care workers allowed information to be gathered and enhance one's knowledge on influenza and its vaccine. Patients

attended clinic have higher chance of exposure to other vaccination measures, such as being recruited to free vaccination programs, introduced to media campaigns, enrolled to the recalls and reminder systems than those who did not. The association between these factors could be confounding or have a modifying effect on each other.

Common limitations of the selected studies

Since most included articles are cross-sectional surveys, recall bias and/or report bias exist. For self-administered questionnaires, misclassification could have occurred due to cultural or religious difference, e.g., the report of having chronic disease(s). Nonetheless, the approach of analysing self-reported data on chronic conditions were reasonably accurate.⁵⁷ The sample was also restricted by the sampling method, e.g., individuals without a home telephone were excluded for telephone interviews.

Relationship between perception, intention and behaviour

People who have positive perceptions towards vaccination or even expressed their interest in receiving the vaccine, does not necessarily lead them to receive the actual vaccination.⁵⁸ A meta-analysis with 47 experimental tests on behavioural intentions and behaviour, concluded that a medium to large change in intention leads to a small to medium change in behaviour.⁵⁹ Even in those intended to get vaccinated, only half had actually been vaccinated.⁶⁰ So there is an anticipatory perception-intention-practice gap and one needs to be cautious and be vigilant for additional components that could contribute to people's practices on vaccination. Thus it was difficult to identify a causal relationship in the cross-sectional surveys. One possible method may be to follow up participants in their actual behaviour afterwards.

Conclusion

This study highlighted that perceptions, advice from doctors/health professionals/family/close friends and free vaccination were changeable factors that are positively associated with influenza vaccination in adults aged 18 to 64 years.

Competing Interests

The authors declare that no competing interests exist.

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Fig 1. Flow diagram of study selection process

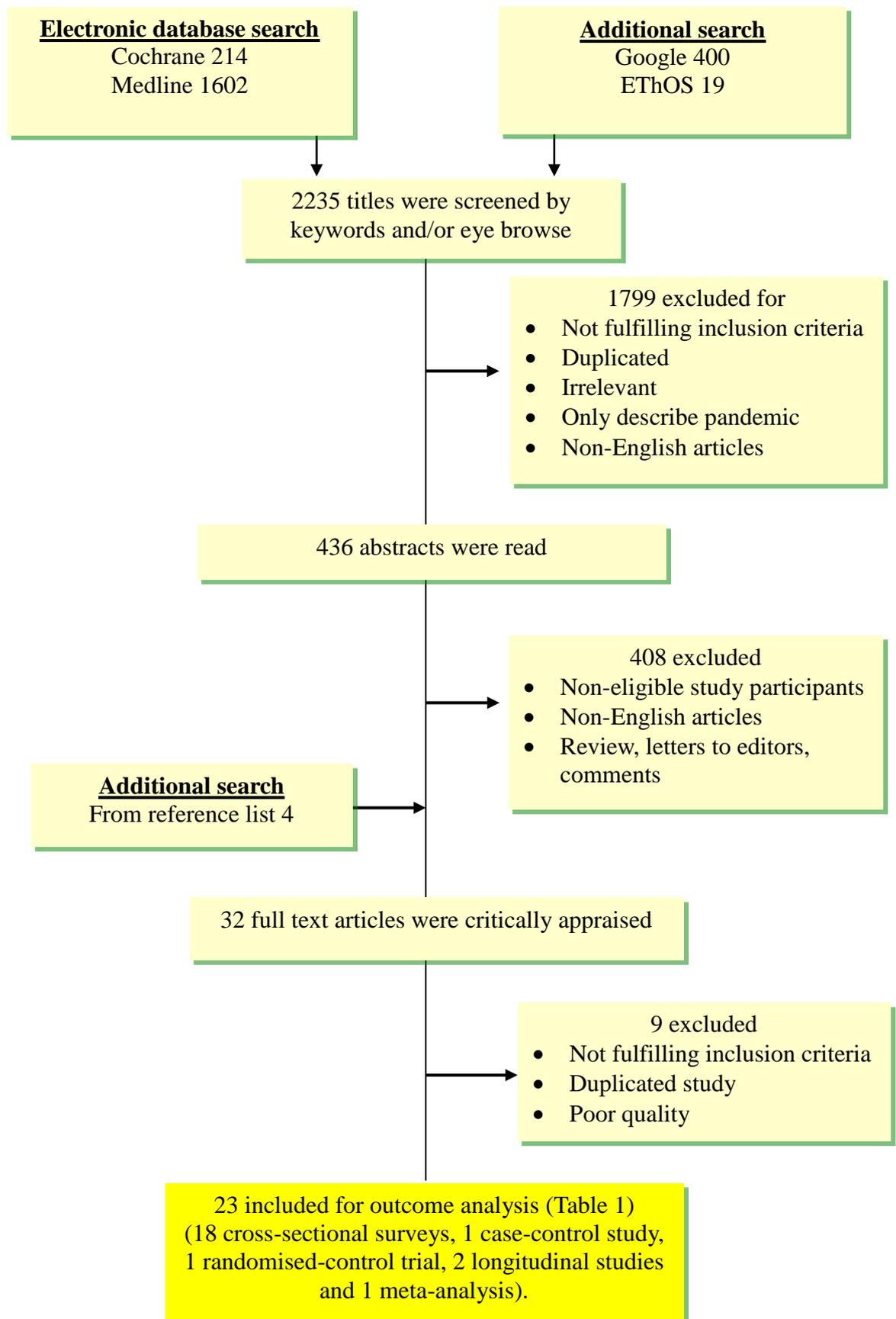


Table 1. Characteristics and key results of the included studies

First author, publication year, place of study	Study design	Participants	Data collection method and date	Key findings: Factors associate with behaviour or intention of receiving influenza vaccine in healthy adults^{††}	Major limitations
Blank et al., ⁶ 2009 (Austria, Czech Republic, France, Finland, Germany, Ireland, Italy, Poland, Portugal, Spain and UK)	Cross-sectional survey	Approximately 1200 to 2000 representative adults per country	Annually repeated population-based surveys (telephone, postal or face-to-face) on influenza vaccination; 2006/07 to 2007/08	The associated factors were being elderly (OR 2.4 -23.7), suffering from a chronic medical condition (OR 1.8 -13.7) or belonging to both of these risk groups drastically enhanced the odds ratios (OR 3.1-120.1) in all countries. Working as health professional was less strongly correlated with influenza vaccination and in some countries non-significant.	Misclassification such as interviewees describing themselves as chronically ill may stem from local differences in the comprehension of the term chronic illness, e.g., due to cultural or religious influences.
Caille-Brillet et al., ³⁰ 2013 France	Longitudinal study	1,451 individuals from 575 households	Data from Cohort for Pandemic Influenza (CoPanFlu); Dec 2009	A moderately negative effect of the 2009/10 pandemic on vaccination behaviours. Amongst the population with no risk factors, the post-pandemic influenza vaccine coverage decreased, with people aged 15 to 24 years and 45 to 64 years being most likely to abandon vaccination.	The CoPanFlu France cohort was originally designed to assess the relative risk of infection by the pH1N1, not the uptake of influenza vaccination.
Carrasco-Garrido et al., ³¹ 2009 Madrid, Spain	Cross-sectional survey	7,341 adults aged 16 and above	Personal, home-based interviews using structured questionnaire; Nov 2004 to Jun 2005	Those who believed they were satisfied with the health services were more likely to receive the vaccine (OR = 1.23). Age (comparing aged 50-64 with 16-49, OR 1.97), chronic conditions (OR 3.9) and visit to a GP for medical consultation (OR1.55) were also associated.	The response rate on the questionnaires was 40%. Self-reporting data were not validated and there was no explanation on checking on validity.
Cassidy et al., ³² 2009 US	Cross-sectional study	1,311 patients attending AED	Interview AED patients and retrieve records; Dec 2005 Mar 2006	Factors associated with vaccination agreement were comorbidity (OR 1.48) and being 50 to 64 years old with prior immunization (OR 2.44). Factors unrelated to vaccination were age, sex, race and pregnancy.	Random interviewer effect was statistically significant. Many who agreed to be immunized (74%) were already vaccinated.
Chapman and Coups, ³³ 1999 US	Cross-sectional survey	79 university employees and 435 corporate employees	Interview and self-administered questionnaire; fall 1997	Factors associated included perceived effectiveness (r = 0.49), likelihood of side effects (r = -0.31), previous flu shot (r = 0.66) and older age (r = 0.10) and percentage of co-workers who also received the shot (r = 0.24).	For the university employees, vaccine acceptors and decliners were recruited in different ways.

^{††} All ORs (Odds ratios) showed are adjusted OR and statistically significant with $p \leq 0.05$, unless otherwise stated

First author, publication year, place of study	Study design	Participants	Data collection method and date	Key findings: Factors associate with behaviour or intention of receiving influenza vaccine in healthy adults^{††}	Major limitations
Chapman and Coups, ³⁴ 1999 US	Cross-sectional survey	412 corporate employees offered a free flu vaccine	Interview and self-administered questionnaire; 1-10 Dec 1997	There was a small relationship (OR 2.38) between vaccination acceptance to monetary time preferences (extent to which one value future outcomes relative to immediate ones). Other variables, such as perceived effectiveness of the vaccine were more predictive.	The relationship between time preferences and vaccination acceptance was weak and inconsistent, although it was statistically significant.
Cohen et al., ³⁵ 2012 New York, US	Cross-sectional, part of a randomised controlled trials (RCT)	2,788 participants from 509 households (contained ≥ 3 people in the household)	20 minute structured interview, 2006/07 and 2007/08 flu seasons	Positively associated factors were female gender, older age, higher education, greater primary respondent knowledge of flu, having been born in the USA, and having a chronic respiratory condition (OR 2.03). The most common reasons for not being vaccinated were the beliefs that vaccination was unnecessary or ineffective.	Data were collected as part of a larger community study of households. Data for all participants were reported by a single household respondent.
Endrich et al., ³⁶ 2009 Austria, Czech Republic, France, Finland, Germany, Ireland, Italy, Poland, Portugal, Spain and UK	Longitudinal survey	92,101 participants from 11 different European countries	Annually repeated population-based surveys (telephone, postal or face-to-face) on influenza vaccination; 2001/02 to 2006/07	Chronic illness was consistently correlated with vaccination across 11 European countries (ORs from 1.38 to 3.06). Belonging to the risk group (aged ≥ 65 years, or suffering from chronic illness or work in the medical field) was the strongest predictor of having received the vaccination (OR 1.94 - 11.83). Other socioeconomic factors (gender, household income, size of household, educational level and population size of living residence) were differently expressed amongst countries.	Information about characteristics of non-responders was lacking. All data collections rely on self-reported information which may be a source of potential error.
Horby PW et al., ³⁷ 2004 Australia	Cross-sectional survey	1,496 people aged 40 to 64 years	Computer-assisted telephone interview; 19 October to 15 November 2001	Independent factors associated with vaccination were: belief that influenza vaccine is effective in preventing influenza (OR 4.8); the presence of chronic disease (OR 1.6); and occupational risk group (OR 2.4).	The response rate was 30%. Bias in excluding household without a fixed telephone and of residents and recall bias.
Hong Kong Medical Association, ³⁸ 2013 Hong Kong, China	Cross-sectional survey	1,013 Cantonese-speaking Hong Kong Citizens of age 18 or above	Web-based Computer Assisted Telephone Interview; 6 to 16 November, 2012	Only 68.4% of people knew influenza vaccination is the most effective means of preventing influenza infection. A large number of respondents believed that taking in more Vitamin C (52%) can help protect them against influenza. Over 80% of people did not know 'herd immunity'.	The data was presented as percentage and without statistical comparison and adjustment.
Lau et al., ³⁹ 2012 Hong Kong, China	Cross-sectional survey	1,102 Hong Kong Chinese adults aged 18-64 years	Random telephone survey; Apr to May 2006	Associated factors included adults of age ≥ 30 years (OR1.91), those who attended university (OR 2.25), health professionals (OR 2.46), knowledge that IV was required annually (OR 1.59), perceiving that influenza could cause severe or very	Individuals without a home telephone were excluded

First author, publication year, place of study	Study design	Participants	Data collection method and date	Key findings: Factors associate with behaviour or intention of receiving influenza vaccine in healthy adults ^{††}	Major limitations
				severe harms (OR, 2.21) and having been recommended by some health professionals to take up IV (OR 5.96).	
Liao et al., ⁴⁰ 2013 Hong Kong, China	Cross-sectional survey	505 Chinese students and employees from a university	Online survey Wave 1: Jan and Mar 2009; Wave 2: Jan and Mar 2010	Feeling at risk was an affective-cognitive dimension of risk perception predicted subsequent vaccine uptake. Chronic conditions (OR 4.55), past vaccine uptake (OR 5.18) and married (OR 2.71) were associated with subsequent vaccine uptake.	Study population was restricted to university students and employees. Low response rate (30%) in Wave 2.
Lin et al., ⁴¹ 2010 US	Randomised cluster trial	2,389 workers aged 18-49	Questionnaire; 2007-2008 vaccination season	Factors associated with previous influenza vaccination were older age (OR 1.06), female, higher education (OR 1.54) and greater support for injectable vaccine (OR 2.34).	The main part of the study was comparing choice of vaccine type (intranasal or injectable).
Looijmans-van den Akker et al., ⁴² 2007 Netherlands	Cross-sectional survey	1,725 Dutch patients age over 50 years random selected in a university medical centre database	Self-administered questionnaire; 2005	No substantial differences in determinants associated with not complying with influenza vaccination between smokers and non-smokers. Most important associated factors of not complying in smokers and non-smokers were patient's beliefs not to be susceptible to disease (OR 4.0 vs 2.8, CI: 2.0, 3.9), finding it difficult to go to the GP for vaccination (OR 2.5 vs OR 1.8) and being against vaccination (OR 2.4 vs 1.8).	The response rate on the questionnaires was 43% on a university medical centre database. There may be differences in intent to comply among heavy and light smokers.
Mok et al., ⁴³ 2006 Hong Kong, China	Cross-sectional survey	452 outpatient clinic patients age ≥18 years, able to read and speak Chinese	Self-administered questionnaire; Sep to Oct 2004	Factors associated with intention to be vaccinated were chronic disease (OR 1.69), having received the flu shot in the previous year (OR 4.06), perceived susceptibility (OR 0.53, and reinforcing factors from family (OR 0.72, non-vaccinated compared to vaccinated) and doctor (OR 0.71).	Limited to recruiting Chinese in an out-patient setting.
Santibanez et al., ⁴⁴ 2010 US	Cross-sectional survey	4,835 participants at 50-64 years old	Telephone survey; Feb to May 2004	Associated factors included age, education level, recent doctor visit (OR 2.0), and beliefs about vaccine effectiveness (OR 2.7), chances of getting sick with the flu (OR 5.4). Beliefs about influenza vaccination varied by race/ethnicity, education, and gender.	Participants' medical conditions were unknown; low random-digital-dial response rate (51%)
Takahashi et al., ⁴⁵ 2002 Japan	Case-control study	98 out-patients age 18 years or above	Telephone interview; Nov 1998 to Feb 1999	Associated factors were recommendation by a family member and/or a close friend (OR 17.74); belief in influenza vaccine efficacy (OR 10.55); having a family member and/or friends who had been vaccinated before (OR 6.44); physician's recommendation (OR 4.03); knowledge about the influenza vaccine (OR 3.06); and fear of adverse reactions (OR 0.21, negative acceptance).	Cases and controls were selected from a single hospital which reduce generalisation of the study. Most of the participants in this study were female and elderly.

First author, publication year, place of study	Study design	Participants	Data collection method and date	Key findings: Factors associate with behaviour or intention of receiving influenza vaccine in healthy adults^{††}	Major limitations
Thomas et al., ⁴⁶ 2011 Multiple (review)	Meta-analysis on randomised controlled trials (RCT)	Forty-four RCTs were included	Meta-analysis with pooled OR and systematic analysis	No recommendations for practice can be drawn from this review. Interventions such as personalized postcard, home visits, reminder to physicians, free vaccine, and financial incentives to physicians were reviewed for those aged 60 years and older in the community.	The quality of most RCTs was graded as at high risk of bias and no recommended intervention was suggested.
Uscher-Pines et al., ⁴⁷ 2010 US	Cross-sectional survey	4,040 adults aged 18 and above	Draw data from a nationally representative survey conducted on March 5-24, 2010	Adults aged 19-49, as newly recommended for influenza vaccination, were less likely to believe flu vaccines were safe (44% vs. 63%); to have ever been vaccinated (36% vs. 64%); to be vaccinated following a health-care provider recommendation (44% vs. 52%); and to visit a doctor's office during vaccination season (41% vs. 69%).	Secondary data was used. Uncertain exactly how the data collection process was done and how well it was done.
Vaux et al., ⁴⁸ 2011 France	Cross-sectional survey	10,091 people from 8,905 households	Telephone survey, May 2009 to April 2010	The main associated factor with seasonal influenza vaccination were at risk group (OR 4.0), university graduate (>2 years) (OR 2.5) and offered free vaccine (OR 4.5). Other factors associated with pandemic vaccination, such as, household with one or two children <5 years and occupation were not a determinant for seasonal influenza vaccine uptake.	This study excluded households without telephone and those with only mobile-telephones. The small numbers in some groups caused wide confidence intervals.
Vlahov et al., ⁴⁹ 2012 New York City, US	Cross-sectional survey	991 participants from medically underserved area	Street-intercept method; 10 min survey; end of the 2009/10 flu season	Factors associated with lack of interest included being black (OR 3.9), uncomfortable with government (OR 2.12), concerned about getting flu (OR 1.62) and no recommendations from health-care providers (OR 1.43)	Uncertain if the OR was adjusted for confounding factors. Bias due to Street-intercept method.
Wada and Smith, ⁵⁰ 2012 Japan	Cross-sectional survey	3,192 Japanese aged 20 to 69 years	Web-based survey for those registered in a web-based survey company	Factors associated with vaccination included vaccination in previous year (OR 3.81), the number of children per household (1 compared with 0; OR 1.37), and household income (\$50,000 to <\$100,000 compared with \$0 to <\$50,000; OR: 1.30). Smoking was inversely associated (OR: 0.79).	The study population was recruited through a web-based survey company, thus introducing recruitment bias.
Wu et al., ⁵¹ 2013 Beijing, China	Cross-sectional survey	13,002 Chinese adults ≥18 years	Interviewers visited the households and conducted face-to-face interview; Jan 2011	The influenza vaccination coverage did not change significantly after the influenza pandemic. Positive associated factors with influenza vaccination included older age and higher level of education vaccination in 2009/2010 and 2010/2011. The most commonly reported reason for non-vaccination was 'I don't think I am very likely to catch the flu' (49.3%).	Odds ratio was not given in the majority of analysis. Given the large sample size, uncertain if this is part of another study.

Table 2. Summary of factors (variables) associated with uptake of influenza vaccination

	Group	Factors ^{††}	Odds Ratio (range of mean OR)
1	Demography	<ul style="list-style-type: none"> - age^{6, 31, 39, 41} - education level^{6, 37, 39, 40, 48} - being health professional^{6, 36, 37, 39} - married⁴⁰ - gender, ethnic origin, income, employment, household size^{6, 36, 48} 	<ul style="list-style-type: none"> - 1.06-23.7 - insignificant / 1.54-2.25 - insignificant / 2.4-4.9 - 2.71 - insignificant or varies
2	Knowledge	<ul style="list-style-type: none"> - knowledge of influenza and influenza vaccination^{39, 45} - knowledge of effective measures to prevent influenza^{37, 45} - knowledge that vaccination was required annually³⁹ - knowledge of influenza vaccine being recommended⁴⁵ - general knowledge on transmission and treatment of influenza and upper-respiratory infections³⁵ 	<ul style="list-style-type: none"> - 1.6-3.3 - 1.59-3.06 - 1.59 - 1.30 - 1.25
3	Needs	<ul style="list-style-type: none"> - presence of chronic disease(s)^{6, 31, 32, 35, 36, 37, 40, 43, 48} - visit to physician recently^{31, 44, 45} - living with children and/or elders^{48, 50} - self-reported health status⁴⁴ 	<ul style="list-style-type: none"> - 1.38-13.7 - insignificant / 1.55-2.0 - insignificant / 1.37 - insignificant
4	Health behaviour	<ul style="list-style-type: none"> - previous influenza vaccination status^{33, 40, 43, 50} - smoking^{42, 50} 	<ul style="list-style-type: none"> - 4.06-5.18 - insignificant / 0.79
5	Belief & perceptions	<ul style="list-style-type: none"> - perceived vaccine efficacy^{37, 44, 45} - perceived vaccine safety and adverse events⁴⁵ - perceived chances of contracting influenza^{44, 49} - perceived health impact of having influenza³⁹ - fear of adverse reactions⁴⁵ - scare about injection⁴⁵ 	<ul style="list-style-type: none"> - 2.7-10.55 - 10.5 - 1.62-5.40 - 2.21 - 0.21 - insignificant
6	Health-Care Systems	<ul style="list-style-type: none"> - free vaccination^{46, 48} - access to health-care settings⁴² - satisfied with the health services³¹ - client reminder system (e.g., telephone, post cards)⁴⁶ 	<ul style="list-style-type: none"> - 4.5-7.8 - 1.8 - 1.23 - inconsistent result
7	Advice & social support	<ul style="list-style-type: none"> - advice from doctors^{6, 31, 45} - advice from health professionals^{31, 45} - advice from family and/or close friends⁴⁵ - cues to action (relative and friends receive vaccine)⁴⁵ 	<ul style="list-style-type: none"> - 4.03-7.82 - 1.23-13.0 - 17.74 - 6.44
8	External environment	<ul style="list-style-type: none"> - pandemics^{30, 51} 	<ul style="list-style-type: none"> - insignificant / moderate negative (i.e., reduce vaccination)

* Findings of 3 selected studies^{34, 38, 47} were not presented in this table but included in the text.

†† All references in black are of high methodology quality and blue of moderate methodology quality.

3.2 Supplementary research details

3.2.1. Search details

The search was performed on 21, 25 and 27 November 2013 on published literature in medical databases EMBASE, MEDLINE (PubMed), Cochrane Library, Google Scholar and Electronic Theses Online Service. A total of 2,235 articles were retrieved and were screened by keywords. The titles of 436 articles were relevant and their abstracts were read. Below were the key words used and the number of articles found in each of the database.

Search results of keyword search in EMBASE and MEDLINE (on 21 Nov 2013)

Step #	Keywords	EMBASE	MEDLINE
1	seasonal influenza vaccine.mp. or *Influenza Vaccines/	15624	13307
2	human.mp.	15852575	2390834
3	accept*.mp.	392682	313130
4	attitude/	54528	39357
5	intent*.mp.	89555	69082
6	perception/ or perception.mp.	227054	249365
7	1 and 2 and 3	524	576
8	1 and 2 and 4	29	5
9	1 and 2 and 5	116	110
10	1 and 2 and 6	132	110
Total		801	801

Search results of keyword search in Cochrane Library (on 21 Nov 2013)

Step #	Keywords					
1	Title, abstract, keywords influenza vaccination					
2	search all text accept*					
3	search all text attitude					
4	search all text intent*					
5	search all text perception					
Result	Reviews	Trials	Methods	Tech Ass ^{§§}	Econ Eva ^{***}	
1 and 2	16	70	0	2	17	
1 and 3	5	28	2	1	0	
1 and 4	21	26	1	1	14	
1 and 5	5	4	1	0	0	
Total		214				

^{§§} Technology Assessments

^{***} Economic Evaluations

Search results of keyword search using Google Scholar (on 25 Nov 2013)

Google scholar <<http://scholar.google.com>> is an engine provides a search of scholarly literature across disciplines and sources, including theses, books, abstracts and articles on the internet. Google Scholar by default listed the fastest searched results. The first 100 results of each of the steps below were browsed. Out of the 400 results, 29 abstracts were read and 3 were included for critical appraisal.

Step #	Keywords	Result
1	Seasonal influenza vaccination and accept*	First 100
2	Seasonal influenza vaccination and attitude	First 100
3	Seasonal influenza vaccination and intent*	First 100
4	Seasonal influenza vaccination and perception	First 100
Total		400

Search results of keyword search using Electronic Theses Online Service (EThOS) (on 27 Nov 2013)

Electronic Theses Online Service (EThOS) is the UK's national thesis database across more than 300,000 theses in over 120 institutions for free search of UK's doctoral research theses. The title and/or abstracts of the 19 theses were read and none was included for critical appraisal.

Step #	Keywords	Result
1	Seasonal influenza vaccination	3
2	Vaccine and accept*	9
3	Vaccine and intent*	3
4	Vaccine and perception	4
Total		19

3.2.2. Critical appraisal of the selected articles

Twenty-three articles were selected and critically appraised for eligibility. These articles were mostly observational studies and surveys. There were 18 cross-sectional surveys, 1 case-control study, 1 randomised-control trial, 2 longitudinal studies, and 1 meta-analysis.

A critical appraisal framework with ten questions was designed to assess the methodological quality of non-randomised trials. Each question represents a methodology quality criterion and one point is scored if that criterion is fulfilled. Therefore a ten is the maximum score which can be given and represents a very high quality study. These questions were formulated with reference to the US CDC Transparent Reporting Evaluations with Nonrandomized Designs¹³⁸ and National Health Service's Critical Appraisal Skills Programme (CASP)¹³⁹ in reviewing the quality of the articles.

Table 5 Review questions as quality assessment tool for critical appraisal

Aspects	Question
Design	1. Was the study design appropriate to answer the research question?
Representativeness	2. Were the study participants representing the target population, i.e., good sampling method to reduce selection bias?
Sample size	3. Was the sample size large enough?
Response rate or loss to follow-up	4. Was the percentage of response rate or loss to follow-up acceptable when compared to other studies? For studies with secondary data analysis, is there a large proportion of missing data?
Validity	5. Was / were data collection tools (questionnaire or others) shown to be valid and reliable?
Outcome	6. Was / were the outcome(s) measurement appropriate?
Reporting	7. Were the absolute and confidence intervals of main primary and secondary result listed to indicate precision?
Confounders	8. Were the confounders adjusted statistically or identified?
Interpretation	9. Was the general interpretation of the results reasonable in the context of study findings and current theory?
Generalisability	10. Could the findings of the study be generalised to the target population (external validity)?

The overall methodological qualities of the articles vary from 4 to 10. The majority of them are moderate to high quality: ten scored 8-10 (high quality); eleven scored 5-7 (moderate quality); and two below 5 (low quality). Nearly all the articles (>90%) presented the studies with a good design, and clearly described the appropriateness and methods of the outcome measures. All the studies have large sample sizes. Some of them had biased samples, low response rates or other reasons which prevented the result to be suitable for generalising to their target populations. Half of the studies did not mention or give enough information on the questionnaire designs, thus losing score on the criterion validity. The two studies scored below 5 were not included in Table 2 'Summary of factors (variables) associated with uptake of influenza vaccination', but their findings are referred to in the text. The assessment result of each article on each critical appraisal criterion is detailed in Table 6.

Table 6 Summary of methodological assessment of the 23 selected studies

Study ^{†††}	Design	Representative	Sample size	Response rate*	Validity	Outcome	Reporting	Confounders	Interpretation	Generalise	Overall score ^{‡‡‡}
Blank et al (2009) ⁶	Y	Y	Y	Y	?	Y	Y	Y	Y	Y	9
Caille-Brillet et al (2013) ³⁰	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	10
Carrasco-Garrido et al (2009) ³¹	Y	Y	Y	N	N	Y	Y	N	Y	Y	7
Cassidy et al (2009) ³²	N	N	Y	Y	Y	Y	Y	N	Y	N	6
Chapman and Coups (1999) ³³	Y	N	Y	Y	Y	Y	N	N	N	N	5
Chapman and Coups (1999) ³⁴	Y	Y	Y	N	N	Y	N	N	N	N	4
Cohen et al (2012) ³⁵	Y	Y	Y	?	Y	Y	N	N	Y	Y	7
Endrich et al (2009) ³⁶	Y	Y	Y	?	Y	Y	Y	Y	Y	Y	9
Horby et al (2005) ³⁷	Y	N	Y	N	?	Y	Y	Y	?	N	5
Hong Kong Medical Association (2013) ³⁸	Y	Y	Y	Y	Y	Y	N	N	Y	Y	8
Lau et al (2012) ³⁹	Y	Y	Y	Y	N	Y	?	Y	Y	N	7

††† () denotes the year of publication

‡‡‡ the highest score is 10

* a response rate lower than 50% is considered unsatisfactory

Y=Yes, N=No, ?=Unknown or insufficient information

Study ^{†††}	Design	Representative	Sample size	Response rate*	Validity	Outcome	Reporting	Confounders	Interpretation	Generalise	Overall score ^{†††}
Liao et al (2013) ⁴⁰	Y	Y	Y	N	Y	Y	Y	Y	Y	N	8
Lin et al (2010) ⁴¹	Y	N	Y	Y	Y	N	Y	N	Y	N	6
Looijmans-van den Akker et al (2007) ⁴²	Y	Y	Y	N	N	Y	Y	N	Y	Y	7
Mok et al (2006) ⁴³	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	10
Santibanez et al (2010) ⁴⁴	Y	Y	Y	Y	?	Y	N	Y	Y	Y	8
Takahashi et al (2002) ⁴⁵	Y	Y	Y	Y	N	Y	Y	Y	Y	N	8
Thomas et al (2011) ⁴⁶	Y	N	Y	Y	Y	Y	Y	Y	Y	N	8
Uscher-Pines et al, (2010) ⁴⁷	Y	Y	Y	?	N	Y	N	N	N	N	4
Vaux et al (2011) ⁴⁸	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	10
Vlahov et al (2012) ⁴⁹	Y	N	Y	?	?	N	Y	?	Y	Y	5
Wada and Smith (2013) ⁵⁰	Y	N	Y	Y	N	Y	Y	Y	Y	N	7
Wu et al (2013) ⁵¹	Y	Y	Y	Y	?	Y	N	N	N	Y	6

4. Design, sample and pilot of Case-control study

In this chapter I describe the design and pilot of my case-control study. It includes the research objective, hypothesis, sample size calculation, sampling method, questionnaire development, and describes the pilot phase implementation and results.

4.1 Research objective, question and hypothesis

Objective

The objective of this study is to determine which factors (variables) are associated with influenza vaccine uptake in residents of Hong Kong aged 50 to 64 years in 2011/12 and 2012/13.

Research question

What were the differences between those residents of Hong Kong aged 50 to 64 years who received influenza vaccine during the period from 2011/12 to 2012/13 and those who did not?

Hypothesis

There were differences in associated factors (variables) between those Hong Kong residents aged 50 to 64 years who received influenza vaccine in 2011/12 and 2012/13, and those who did not.

Null hypothesis

There were no differences in associated factors (variables) between those Hong Kong residents aged 50 to 64 years who received influenza vaccine in 2011/12 and 2012/13, and those who did not.

4.2 Sample size calculation

The calculation of sample size was undertaken according to the formula proposed by Fleiss for unmatched case-control study with dichotomous exposure variable.^{140,141,142} The software Epi Info was used for sample size calculation. The sample size was calculated with a significance level of 0.05 and a power level of 80%. With odds ratio (OR) 2.07, case to control ratio 1:2, and the percentage of exposure in control 10%, it was estimated that **551 participants** (184 cases and 367 controls) were required. The estimated response rate was 50% and at least 1,102 people had to be approached for data collection.

Fleiss formula

$$n_1 = \{Z_{\alpha/2}\sqrt{[(r+1)\bar{p}\bar{q}]} + Z_{1-\beta}\sqrt{(rp_1q_1 + p_0q_0)}\}^2 / [r(p_1-p_0)]^2$$

n_1 : number of exposed, n_2 : number of unexposed; $n_2=rn_1$

r : allocation ratio of referent to study group size

$$\bar{p}\bar{q} = (p_1+rp_2)/(r+1)$$

$$\bar{q} = 1 - \bar{p}$$

$Z_{\alpha/2}$: standard normal deviate corresponding to the probability of an alpha error=5%

$Z_{1-\beta}$: standard normal deviate corresponding to a power of $1-\beta=80\%$

R : ratio of unexposed to exposed

p_1 : proportion of exposed with disease and $q_1=1-p_1$

p_0 : proportion of exposed without disease and $q_2=1-p_2$

Assumptions:

- i. OR under the null hypothesis, $OR_0=1$
- ii. Anticipatory OR, $OR_a=2.07$
- iii. Alternative hypothesis (for two-sided test), $OR \neq 1$
- iv. Exposure in control=10%

Effect size

The effect size referred to the OR of previous studies in my systematic literature review.^{§§§} The list of variables positively associated with influenza vaccination with OR ranged from 2.07 to 18.7. One factor – fear of adverse reactions – was negatively associated with influenza vaccination, with an OR of 0.21. Therefore an OR of 2.07 has been used to calculate the sample size required.

^{§§§} The systematic literature review presented in Chapter 3 in this thesis was updated on November 2013. The ORs used for this sample size calculation was based on the previous version of the review done on March 2013.

Exposure

A low percentage of exposure in control (10%) was chosen to allow for a larger sample size, and account for unknown probabilities in most factors in the control. Here, the term 'exposure' refers to factors or variables associated with the uptake of vaccination. Most 'exposure' factors (variables) in this study were beliefs or perceptions rather than external exposures. There are 38 variables and their probability in the control group varies.

Power

Although there is no formal standard for power, by convention a power of 80% is used in many studies. Therefore 80% was chosen to determine the sample size. Besides, different values of power (e.g., 80%, 85% and 90%) were applied to explore and scope the required sample size. For a power of 90%, 749 people would be required. For a power of 80%, 551 people (184 cases and 367 controls) were required.

Response rate

In some well-designed health surveys on vaccination conducted in Hong Kong, the response rates ranged from 72.4% to 80%.^{128,143} A study concluded that the average response rate of different kinds of surveys was around 55%.¹⁴⁴ To allow for the uncertainty in the actual response rate, a lower percentage of 50% was selected for sample size calculation. During the pilot, the ratio of total participants to non-participants was around 1 to 2, i.e., one successful interview when two people were asked. Therefore at least 1,102 people had to be approached during data collection.

Case to control ratio

The case to control ratio is 1:2. This was chosen because of the small number of cases available for the study. In the general population aged 18 or above, 14% received influenza vaccination in the past 12 months.³⁸ There were 1.56 million 50 to 64 year olds in Hong Kong in 2011, constituting 22% of the population.⁹⁹ During the pilot, most time was spent in identifying eligible cases. This chosen ratio was selected after consideration of the time, cost and manpower available.

4.3 Sampling

Participants were randomly recruited using street-intercept technique. This technique allowed a large number of eligible subjects to be screened and approached.

4.3.1. Target and sampled population

The target population was adults aged 50 to 64 years living in Hong Kong. The sampled population was adults aged 50 to 64 years living in Hong Kong, recruited in the 6 selected districts during the random time slots. The cases were adults aged 50 to 64 years who received influenza vaccination in 2011/12 or 2012/13, while controls were the same as cases, except they did not receive the vaccine during the same period.

4.3.2. Selection of sampling districts and venues

The population census in Hong Kong is collected based on 18 district council districts. For logistics and manpower convenience, 6 districts were selected for the street intercept interview. In order to choose representative districts, districts were screened based on household incomes¹⁴⁵, median age¹⁴⁶ and highest education level attained¹⁴⁷, as indicated by the 2011 Population Census. The districts with lowest, mean and highest household incomes, median age and highest education level attained have been included. These districts are Kwun Tong, Sha Tin, Tai Po, Wan Chai, Wong Tai Sin and Yuen Long. Southern and Islands districts were excluded because of travel difficulty.

Table 7 District with the lowest, median and highest household incomes, median age and education level

	Lowest	Mean	Highest
Median monthly household incomes	Kwun Tong, Wong Tai Sin	Tai Po, Southern, Islands	Wan Chai
Median age	Yuen Long	Sha Tin	Wong Tai Sin
Median highest education level	Wong Tai Sin	Sha Tin	Wan Chai

After selecting the 6 districts, site visits took place in June 2013 to decide on suitable venues for interviews. Two high-traffic venues near underground train

stations and shopping malls were selected from each district. The selections were based on the potential number of eligible subjects who could be recruited at each venue. For each time slot, one to three interviewers was deployed to each district and they worked at the same venue or at different venues, depending on the availability of eligible subjects they encountered on the street.

4.3.3. Interview schedule

The fieldwork covered weekday office-hours, weekday evenings and weekends to avoid over-representation of participants who are unemployed. A random time slot (morning, afternoon or evening) and dates from 15 July to 15 August 2013 were generated using software Microsoft Excel and agreed to by the interviewers.

Table 8 Interview timetable

Location	Date		Time	Hours	No. of interviewers	No. of interviews
Kwun Tong	27/07/2013	Sat	9:00 -- 13:00	4.0	3	46
	06/08/2013	Tue	9:00 -- 12:00	3.0	2	11
	07/08/2013	Wed	13:00 -- 17:30	4.5	2	59
	12/08/2013	Mon	9:00 -- 12:00	3.0	3	9
Shatin	04/08/2013	Sun	13:00 -- 18:00	5.0	3	76
	05/08/2013	Mon	17:00 -- 21:00	4.0	1	9
	06/08/2013	Tue	12:00 -- 21:00	9.0	1	22
Tai Po	03/08/2013	Sat	15:00 -- 19:00	4.0	3	73
	08/08/2013	Thur	9:00 -- 17:00	8.0	3	19
	11/08/2013	Sun	13:00 -- 17:00	4.0	3	14
	12/08/2013	Mon	16:00 -- 20:00	4.0	1	8
Wan Chai	21/07/2013	Sun	10:00 -- 18:00	8.0	3	33
	30/07/2013	Tue	16:00 -- 20:00	4.0	3	49
	08/08/2013	Thur	14:00 -- 18:00	4.0	1	12
	13/08/2013	Tue	9:00 -- 13:00	4.0	1	8
	15/08/2013	Thur	14:00 -- 19:00	5.0	1	10
Wong Tai Sin	25/07/2013	Thur	9:00 -- 12:00	3.0	2	20
	02/08/2013	Fri	14:00 -- 17:30	3.5	3	57
	09/08/2013	Fri	14:00 -- 21:30	7.5	1	20
Yuen Long	17/07/2013	Wed	14:00 -- 17:00	3.0	2	10
	10/08/2013	Sat	9:00 -- 12:30	3.5	3	20
	11/08/2013	Sun	14:00 -- 20:00	6.0	1	21

The same number of cases and controls were to be recruited in each district. The estimated minimum sample size was 551 and 92 successful interviews, with 31

cases and 62 controls from each district. If the number of participants was fewer than the targeted number in a district, the interviewers would recruit more participants in the next scheduled visit in the same district. If at the end an insufficient number of respondents were recruited in one district, the remaining interviews required would be added to the next scheduled visit to the next district.

In each time slot, one to three interviewers would be deployed to each district. The interviewers were stationed in areas of high pedestrian traffic, such as near underground train stations and shopping malls, during the random time slot assigned. A total of 210 man-hours were spent on collecting the interviews, and a total of 616 interviews were completed.

4.3.4. Interviewer training

Interviews were conducted by four trained research interviewers who were fluent in Chinese and English and who had at least one year telephone interview or street polling hands-on interview experience. I held one briefing session for the interviewers on 28 May 2013. In the briefing, I explained the research details and trained the interviewers on the interviewing techniques. I talked about research design, case and control definitions, procedures and completion of questionnaire. We also discussed how to make initial contacts, how to identify eligible respondents, how to obtain consent, and how to avoid influencing or biasing responses.

4.3.5. Interview procedures

During the assigned date and time, the interviewer approached every adult who appeared to be 50 to 64 years old. Interviewers identified themselves and asked the eligible subject whether they wanted to participate in a 10-minute interview. To determine their eligibility, subjects were asked their age and their residence status. Then the interviewers informed the participants about the nature and purpose of the study, and invited their voluntary participation. Spoken or written consent from respondents was obtained for all the interviews. The interviewer asked and documented all the questions listed in the questionnaire using pen and paper, and checked its completeness before approaching the next participant.

4.4 Questionnaire

Questionnaire development

The questionnaire was designed with the purpose of seeking information on factors (variables) associated with the uptake of influenza vaccination. The questionnaire construction involved the following steps:^{148,149,150}

1. Search for relevant validated and published survey instrument
2. Review questionnaires in related studies and surveys
3. Specify domains and items based on the systematic literature review result
4. Draft questionnaire
5. Translate questionnaire from English to Chinese
6. Seek advice from a panel of experts
7. Pilot the questionnaire
8. Revise and agree on the final questionnaire

The questionnaire is in Annex 1.

Content

A search was done for validated survey instruments. There were well-designed questionnaires for people's acceptance of influenza vaccine but most of these were not publicly available or had a different focus which was not best suited for this study.^{35,38, 151} Reference were taken from several questionnaires on influenza vaccination designed by health authorities (e.g., DH¹²⁸, ECDC¹⁵²).

The content of the questionnaire was determined by the systematic literature review on factors (variables) associated with the uptake of influenza vaccination. There were 38 factors (variables) identified which were then grouped into 8 domains. The 8 domains were: predisposing demography (9 variables); knowledge (5 variables); need (3 variables); health behaviour (4 variables); belief and perceptions (7 variables); health-care system (6 variables); advice and social support (3 variables) and external environment (1 variable). The domains and variables are listed in Annex 2.

The questionnaire consisted of 38 questions: 11 on demography and 29 covered all the factors (variables). The questions were predominantly multiple choice. The five-point Likert-type scale was adopted for grading in 4 questions. The demographic questions were positioned at the start of the questionnaire to screen for suitable participants and serve as a warm-up.

Language and translation

The questionnaire was printed in Chinese and English with language set at primary education level. More than 95% of people aged 50 to 64 years in Hong Kong are Chinese and 75% have attained primary education level or above.⁹⁹ The questionnaire was originally written in English because the questions in the references for the questionnaire were in English. It was then translated by two separate bilingual translators from English into Chinese.

Review by experts

The draft questionnaire was sent to a panel for comment and feedback. The panel comprised of 5 experts: 1 public health physician at the DH Vaccination Office, 1 infectious disease specialist, 2 general practitioners and 1 statistician. The panel was asked to comment on the content and face validity, the relevance of the variables and whether the English and Chinese wordings conferred the same message. Feedback from the experts was obtained through telephone conversations. Most of the advice given by the experts was accepted. Before the pilot, the panel validated the whole questionnaire and confirmed their agreement with all the questions.

Pilot of the questionnaire

There were 29 respondents during pilot. Each respondent was approached by two interviewers at the same time. During the interview, one interviewer communicated with the respondents and filled in the questionnaire, while the other interviewer observed and marked down the respondent's reactions and queries. After completing the questionnaire, the respondents were asked about the clarity, ease of comprehension, relevance to the topics and length of the questionnaire.

A debriefing meeting with the interviewers was held on 2 July 2013. Feedback from interviewers and respondents had provided key information for modifying and finalising the questionnaire. Most interviewers asserted that the questionnaire was too long, as it took up to 15 minutes to complete one questionnaire, and that there were also redundant and ambiguous questions. The questions were then regrouped and their orders relocated, while unclear and ambiguous questions were rephrased or their wordings were clarified.

4.5 Pilot

A pilot study of 29 participants (15 cases and 14 controls) was conducted on the 20 and 22 June 2013 at Lam Tin and Sha Tin districts respectively. In both districts, venues near train stations were chosen because of the large number of pedestrians. I conducted the interviews with the assistance of two additional interviewers. The aim of the pilot study was to test the logistics, pilot the questionnaire, estimate the effect size and sample size, and observe interviewers' practice and skills.

The time required and the response rate was documented to estimate the actual manpower and time needed for data collection. On average, 12 minutes was required to finish one questionnaire. The interview time of the questionnaire interview time for each respondent ranged from 4 to 15 minutes. Most time was spent identifying cases, while controls were readily available. Approximately every one in two to three person asked agreed to be interviewed. The data collected was the entered into an Excel spreadsheet by the interviewers.

A debriefing meeting with the interviewers was held on 2 July 2013 following completion of the pilot, to collect feedback and discuss improvement measures. The pilot demonstrated a street intercept sampling method was feasible and practical for recruiting cases within reasonable constraints of time and effort. This was despite there being no incentive for respondents to take the questionnaire. The pilot established the procedures and steps of the interview process, and also provided useful information for the questionnaire development and improvement of data entry logistics. The pilot study had limited statistical power, the results it provided were inconclusive; it was not comparable to the associations of the variables in the previous systematic review. The sample size calculation remained unchanged; as there were no changes in the effect size, response rate and other parameters in the calculation. Data collected from the pilot study was not included in the case-control analysis.

4.6 Data entry and quality control

4.6.1. Data entry

The categorical variables in the questionnaires were coded and entered into spreadsheet using Microsoft Excel. The coding and Excel spreadsheet were designed by the research student. The data was then entered by five data entry assistance, with four of them also being interviewers. The data entry and rechecking process lasted for three months, from July to September 2013.

4.6.2. Quality control

The two most frequently referred to data quality attributes are accuracy and completeness.¹⁵³ To ensure accuracy, logical consistency was ensured by limiting data entry and setting the data validation dialog box in the Excel spreadsheet. A coding guide, listing all the code that was produced, was distributed to data entry assistants for reference during data entry. The study design and input variables of the study were explained to the data entry assistants prior to undertaking the task. Misinterpretation of the information in the original documents was minimised because all the multiple choice answers were coded. If there was uncertainty, such as ambiguous hand-writing or uncertainty in the entry, the data entry assistant would discuss the issue with their supervisor.

Ten percent of the questionnaires entered were randomly checked by an independent observer (the supervisor). First, a random checklist was generated by Excel, then a data entry assistant would follow the Excel random list and re-enter the questionnaire data. The supervisor would then double-check this double-entry and compare the result with the hard-copy and the first set of data entered. If a high percentage (>20%) of inconsistency was found in any questionnaire, the data entry assistant who entered the questionnaire would be identified. No high percentage of inconsistency was found during the rechecking.

To ensure completeness, any questionnaire with important information or more than 20% of the questions missing was excluded. There were 12 questionnaires excluded because of missing important data, such as year of birth. No questionnaire was excluded because of incompleteness or inconsistency.

5. Case-control study (Research paper 2)

5.1 Research paper 2

Title: Factors associated with uptake of influenza vaccine in people aged 50 to 64 years in Hong Kong: A case-control study

Author(s): May PS YEUNG, Richard COKER

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Candidate's role: All the data presented in this paper was collected through a case-control study of which I was the principal investigator. I generated the research framework and methods; drafted research protocols and questionnaires; identified, analysed and interpreted the data; and wrote and revised the paper.

Keywords: 50 to 64 years, influenza vaccine uptake, Hong Kong, case-control study, associated factors

Word count abstract: 296

Abstract

Background

In Hong Kong, people aged 50 to 64 were added as recommended priority group (recommended group) for influenza vaccination by the Department of Health (DH) starting from 2011/12 onwards. The coverage rate of influenza vaccine for this age group was suboptimal at 8.5% in 2012/13.

Objective

To determine which factors were associated with uptake of influenza vaccination amongst adults in Hong Kong aged 50 to 64 years.

Methods

A case-control study was conducted in communities by street intercept interview from 17 July to 15 August 2013. Cases were adult age 50 to 64 years who received influenza vaccine in 2011/12 or 2012/13, while controls were the same as cases, except they did not receive influenza vaccine in 2011/12 or 2012/13. Multinomial logistic regression analysis was performed on the data to explore the associations between vaccination status and the variables.

Results

A total of 604 respondents were interviewed and included in the analysis. There were 193 cases (vaccinated) and 411 controls (non-vaccinated), with a case-to-control ratio of 1:2.1. When compared, the following were strongly associated with vaccination compared to other factors: 'eligible for free government vaccine' (OR6.38, 95% CI, 3.43-11.87, $p<0.001$); 'willing to receive flu vaccination for free' (OR4.84, 95% CI, 2.13-11.03, $p<0.001$); 'perceived having severe or moderate symptoms when contracting flu' (OR2.90, 95% CI, 1.21-6.97, $p=0.02$), and 'convenient to reach a vaccination location' (OR2.87, 95% CI, 1.06-7.74, $p=0.04$). The majority (89%) of all the respondents were not aware that they belonged to a recommended group for influenza vaccination and most (>80%) were willing to be vaccinated if it was free.

Conclusion

Factors related to the existing health-care service, advice from health professionals, and perception on influenza vaccination had a comparatively strong association with influenza vaccination uptake amongst 50 to 64 year-olds, compared to other factors.

Introduction

Seasonal influenza vaccination (referred to as ‘influenza vaccination’, ‘vaccination’ or ‘vaccine’ below) remains an effective measure to protect individuals and communities from severe morbidity and mortality induced by influenza. To mitigate the disease burden of influenza, many developed countries recommend vaccination for high-risk groups such as children, elders, health-care workers, pregnant women, and people with chronic diseases. The upper age limit for elders differs and most countries do not include adults aged below 60 without other risk indications as a recommended group for vaccination.^{1,2} Some exceptions include the US, Austria and Estonia, who recommend that people aged 6-months or above receive influenza vaccination.³⁻⁵

Meta-analysis and literature review demonstrated that the influenza vaccine has a moderate effect in reducing clinical symptoms of influenza in healthy people from 16 to 64 years.^{6,7} The vaccine efficacy could be up to 70% in healthy adults when content matched WHO recommendations and circulating strain.^{6,8} Vaccine also reduced working days lost and physician visits.^{7,9,10} Local cost-effectiveness studies on influenza vaccination estimated the cost-benefit ratio to be 3.8:1^{****} amongst the working class.¹¹ Although the vaccine did not provide an overall economic benefit in the community, it has yielded significant health benefit by reducing severe complications from influenza.^{5,12,13} Many middle-aged adults have undiagnosed medical conditions such as diabetes mellitus and they are at higher risk of severe influenza related complications.^{14,15}

Hong Kong, situated in Southeast China, has become vigilant against influenza and respiratory infectious diseases, particularly following avian influenza, SARS and pandemic influenza H1N1 in 2009. Beginning in 2011/12, people aged 50 to 64 were added as recommended group for influenza vaccination by the Department of Health (DH).¹⁶ The influenza vaccination coverage rate of this age group in 2012/13 was 8.5%¹⁷, while previous data was unavailable. As a reference, 13% of those aged 18 to 64 years in the general population had the

**** By proportion HK\$3.8 spent on vaccination can save HK\$1 because influenza-like illness has been prevented.

influenza vaccination in the previous 12 months in 2007.¹⁸ The corresponding influenza vaccine coverage rates of this age band in the United States (US) was 45.1% in 2012/13, and 22% in the UK in 2003/4.^{19, 20}

A change in the influenza vaccination recommendation and policy was initiated by DH. In January 2011, an increase in the number of hospital admissions due to influenza among persons aged 15 to 64 years was observed. Subsequent local epidemiological studies showed there was a real increase in Intensive Care Unit (ICU) or fatal influenza cases in healthy individuals aged 50 to 64 years, with an incidence of 1.8 per 100,000 population. This incidence was higher than the corresponding incidences in any other age group, including young children aged below 6 years (0.7 per 100,000) and elders over 65 (0.6 per 100,000). Also, the largest percentage (41%) of influenza-related deaths during this period were from persons aged 50 to 64 years.¹⁶

The increase in ILI activity and hospital admission was possibly accounted for by the influenza A(H1N1)pdm09 being the dominant circulating virus (~90% of all influenza isolates) during the winter of 2010/11.²¹ A review on international epidemiology reported that the influenza A(H1N1)pdm09 disproportionately affected and increased hospitalisation and death in adults aged below 65.²²⁻²⁴ Some observers postulated that the discrepancy was because some elderly might have cross-immunity to influenza A(H1N1)pdm09 due to past influenza infection.

Following review and discussion, DH recommended that doctors vaccinate healthy people aged 50 to 64 based on the local context. There was a likelihood that influenza A(H1N1)pdm09 virus would continue to circulate and vaccination is considered to offer good protection against clinical influenza.²⁵ No free or subsidized influenza vaccination service was provided by the Government to this group, except those who already belonged to the high-risk group and those with financial difficulties, i.e., Comprehensive Social Security Assistance (CSSA) receivers. Healthy 50 to 64 year-olds, without other risk indicators, had to pay out-of-pocket if they want to be vaccinated.²⁶

After this new vaccination service was launched in 2011/12, vaccination coverage was low (8.5%) in this new target group. This study aimed to determine which factors were associated with the uptake of influenza vaccination amongst people aged 50 to 64 years in Hong Kong.

Method

A case-control study was conducted in a community setting in Hong Kong from 17 July to 15 August 2013. Street intercept interview were undertaken in 6 districts (out of a total of 18). In order to recruit a representative sample of the population, districts with the lowest, median and highest household incomes, median age and education levels were chosen according to the 2011 Population Census.²⁷ The selected districts were: Kwun Tong, Sha Tin, Tai Po, Wan Chai, Wong Tai Sin and Yuen Long. The interviewers were assigned a random time slot, covering weekday, weekends, office and non-office hours.

Cases and controls

Cases were (i) those who received influenza vaccine in 2011/12 or 2012/13, i.e., from 1 September 2011 to 31 August 2013^{††††}; (ii) aged 50 to 64 years in 2012 to 2013 (i.e., born between year 1949 to 1962); and (iii) citizens who were resident in Hong Kong.

Controls were the same as cases in (ii) and (iii), except they did not receive influenza vaccine in 2011/12 or 2012/13. Some controls had received influenza vaccine before 1 September 2011. They were classified as control because they were not recommended group under the previous vaccination policy.

Inclusion and exclusion criteria

Cases and controls were included if they:

- Fulfilled the definitions; and
- Agreed by oral or written consent; and
- Understood spoken or written Chinese or English.

^{††††} Most influenza vaccines expire before August in each year. Influenza vaccines of next season usually are available to doctors in early September. The Government Vaccination Programme started in early November in the previous 5 years since 2008/09.

Cases and controls were excluded if they refused to participate, were travellers, or were not eligible for influenza vaccination due to medical contraindication.

Sample size

The sample size was calculated with a significance level of 0.05 (two-sided) and a power level of 0.80. From a search of the literature, the effect size (odds ratios, OR) of factors associated with influenza vaccination varied from 0.2 to 18.7. The calculation of sample size was done by the Fleiss formula for unmatched case-control study with dichotomous exposure variable.²⁸ A minimum sample size of 551 (cases and controls) was required. To allow for the uncertainty, 50% was used for sample size calculation. It was estimated that at least 1,102 people had to be approached.

Data collection

The questionnaire was conducted in the summer 2013 before the next influenza vaccination season, which usually begins in September of each year.

Primary data was collected by four trained research interviewers who were fluent in Chinese and English and who had at least one year's experience carrying out hands-on interviews. In each time slot, one to three interviewers would be deployed to each district. The interviewers were stationed in areas of high pedestrian traffic, such as near underground train stations and shopping malls, during the random time slot assigned. A total of 210 man-hours were spent on the interviews.

Before each interview, the interviewer would inform the respondent about the nature and purpose of the study and invited their voluntary participation. Interviewees were asked to respond only after informed consent was obtained. The interviewers would ask the respondents questions, document all the questions in the questionnaire form using pen and paper, and check its completeness before approaching the next person.

Hypothesis and Null hypothesis

There were differences in associated factors (variables) between those Hong Kong residence aged 50 to 64 years who received influenza vaccine in 2011/12 and 2012/13, and those who did not. The Null hypothesis assumes no such association.

Pilot

A pilot study of 29 respondents (15 cases and 14 controls) was done on the 20 and 22 June 2013. It was conducted by three interviewers in two districts. After filling in the questionnaire, respondents' feedback was collected on the clarity, ease of comprehension, relevance to the intended topics and length of the questionnaire. The pilot tested the logistics and issues related to the questionnaire; estimated the manpower required; the effect size and sample size; and provided an opportunity for interviewers to familiarise themselves with the arrangements.

After the pilot was completed, a debriefing meeting was held with the interviewers on 2 July 2013. Feedback and suggestions from interviewers were adopted to enhance and finalise the interview process and the questionnaire. The data collected from the pilot study was not included as part of the results section in the report.

Questionnaire design

The questionnaire was designed with reference to past vaccination questionnaires from health authorities^{29, 30} and relevant studies.³¹⁻³³ The draft questionnaire was then sent for comment to a multi-disciplinary team, comprised of an infectious disease specialist, an epidemiologist and general practitioners. The questionnaire was in Chinese and English and it had 38 questions including 11 on demographic data and 27 covering the factors (variables) to be examined. The demographic questions were placed at the start of the questionnaire to screen for suitable subject and serve as a warm-up. The questions were predominantly multiple choice, while the five-point Likert-type scale was adopted for grading in 4 questions. Questions were grouped in 8 content domains – demography, knowledge, health need, health behaviour, belief and perceptions, health-care system, advice and social support, and external environment – for easy comparison of variables.

Data management

Logical consistency was ensured by limiting data entry and selecting data validation in the data entry software. In addition, at least 10% of the questionnaires entered were randomly checked using double entry method by an independent observer. Twelve questionnaires were excluded after checking for completeness, inconsistency or with important data missing, e.g., year of birth.

Statistical analysis

Statistical analyses were performed using the software SAS 9.3. Categorical demographic data and variables were compared using Pearson chi-square test, crude and adjusted odds ratios (ORs) with corresponding 95% confidence intervals (CIs) and p-values. For categorical data with any of the cells with an absolute number fewer than 5, Fisher's exact test was used. Any variables with p values <0.25 and those with important associations demonstrated in the literature were selected for multinomial regression analysis (backward stepwise regression algorithms). The regression model is a built-in formula in the SAS software. All statistical tests were two-tailed and variables were considered significant at a significance level of 0.05.

Result

The study included 193 cases (vaccinated) and 411 controls (non-vaccinated), with a case to control ratio of 1:2.1. The average interview time was 7 minutes (standard deviation ± 4 minutes) for each questionnaire, and the response rate was 41.7%.

1. Demography

Baseline demographic data of cases and controls were compared using Pearson Chi-Square Test and odds ratios. The differences between the two groups were statistically insignificant on sex, ethics, education level, employment status, personal monthly income, current smoking and drinking status. There was no statistically significant OR after statistical adjustment, indicating no associations was found between vaccination and any of the chosen demographic variables. The demography of cases and controls are in Table 1.

The majority of the respondents were Chinese, and there were more female than male respondents (38.4% vs 61.6%). Most (86.5%) of those who had an occupation were aged 59 or below. Overall, half of the respondents (51.5%) had no income. Similarly half of the respondents (53.5%) were unemployed, retired or housewives. One in four (26.3%) were housewives; and one fifth (20.03%) were retired. The majority of them (71.5%) received at least 9 years education up to the secondary level.

There was a slight increasing trend of vaccination in the 55 to 59 group (crude OR^{****} 1.58, 95% CI 1.03-2.41, p=0.04) and 60 to 64 group (crude OR 1.83, 95% CI 1.20-2.77, p=0.005) when compared to the 50 to 54 group. However, the adjusted ORs for both age groups were insignificant.

Comparing cases and controls, people who were health professionals (crude OR 3.3, 95% CI 1.16-9.41, p=0.03) and social security CSSA recipients (crude OR 2.7, 95% CI 1.10-6.63, p=0.03), more commonly received the vaccine than those who were not. However, there were only 15 health professionals and 20 CSSA recipients in the respondents, and it may not be valid to conclude there were associations of these two variables with vaccination given their low representation.

The sample was also compared to the actual district population by age and sex to check for representativeness. In the sampled respondents, there was proportionally higher numbers of females, particularly in the 50 to 54 and 55 to 59 age groups, in most of the sampled districts. This study included more females than males by proportion (M:F = 1:1.6), while the overall male to female ratio in the target community was 1:1. Other demographic parameters of the sampled population such as the age proportion between groups, education level, ethnicity, and the percentage of employment, were comparable to the target population (ie., Hong Kong general population aged 50 to 64 years). There was no apparent discrepancy of the sample and the target population.

^{****} All odds ratios (ORs) mentioned in the text of this article are statistically adjusted ORs, unless otherwise stated as crude odds ratio (crude OR).

2. Health knowledge related to influenza vaccine

The majority (89%) of all the respondents were aware that they were recommended for influenza vaccination by DH. However, the cases were more aware themselves of being recommended for influenza vaccination than the controls, (OR2.34, 95% CI 1.23-4.44, $p=0.009$). There were health knowledge differences between the cases and controls in all the questions asked on knowledge, including government vaccination services, vaccine reduction in influenza-related hospital admission, and vaccine protection to healthy adult. However, these associations were statistically insignificant after the OR was adjusted.

3. Health needs

When compared to controls, more cases had chronic diseases; more frequently 'visited doctors in the past 3 months' and 'lived with children below 6 years or elders above 65 years'. However, none of these associations were statistically significant after the OR was adjusted.

4. Health behaviours

There was no association between vaccination and smoking/drinking. Most cases (85.4%) expressed they were likely or very likely to receive the vaccine in 2013/14, compared to only 29.4% amongst the controls. This implies those who had previous vaccinations in 2010/11 and 2011/12 would choose to get vaccinated again in the coming future.

5. Health belief and perception

In general, more cases perceived there to be a higher chance of contracting influenza in the next 12 months and/or having severe influenza or moderate symptoms when compared to the controls. Vaccination was perceived more positively by the cases than the controls. More cases than controls 'perceived flu vaccine to be safe' and 'believed flu vaccine has additional benefits other than flu protection'. More controls than cases perceived the vaccine may lead to severe adverse events, and believed themselves to have good health. However, the only statistically significant variable was 'perception of severe or moderate symptoms when contracting flu' with an OR of 2.90 (95% CI 1.21-6.97, $p=0.02$).

6. Health-care system

There was an association between ‘eligible for free government vaccine’ and vaccination (OR6.38, 95% CI 3.43-11.87, $p<0.001$). When compared with controls, more cases were ‘willing to receive flu vaccination for free’ (OR4.84, 95% CI 2.13-11.03, $p<0.001$). Nearly sixty percent (59.3%) of all the respondents were ‘willing to receive flu vaccination for free’ 36.8% were ‘willing to pay for flu vaccine is below HKD\$50 (USD\$6.4)’ respectively. The percentage of the amount willing to pay for an influenza vaccine was similar between the cases and the controls.

Cases had a higher likelihood of being able to access a convenient location for vaccination (OR2.87, 95% CI 1.06-7.74, $p=0.04$). Fewer cases preferred to go to public clinic for injection (OR0.35, 95% CI 0.22-0.55, $p<0.001$). There were no associations between differences in response to the government telephone reminder service for vaccination, if there was one.

7. Advice

There was a stronger influence of other’s opinion and action on the cases than for the controls in respect to vaccination. When compared, more cases would ‘accept advice from health professionals’ (OR2.67, 95% CI 1.19-5.99, $p=0.02$); and ‘had family members receive flu vaccine’ than the controls (OR2.47, 95% CI 1.54-3.95, $p<0.001$).

8. External factors

External factors refer to unpredictable environmental factors, such as the occurrence of disease epidemics like SARS or pandemic influenza. High percentages of both cases (94.8%) and controls (81.3%) would receive a vaccine when there was a disease epidemic. When compared, more cases would receive a vaccine during an epidemic and the OR was 2.40 (95% CI 1.07-5.37, $p=0.03$).

Additional information

Amongst the controls (i.e., never received vaccination or received vaccine on or before 2009/10), 25.6% of them had received vaccine before. Common reasons for not receiving a vaccine in the controls were: considered vaccination

unnecessary (70.8%); believed they were not in a high-risk group (37.0%); and concern about side effects of vaccination (19.0%). Of the controls that had previously been vaccinated, 59% had received the vaccine at a public clinic. Responses to the multiple answer questions are in Table 3.

Discussion

Study design and sampling method

This is a case-control study with vaccination status as the ‘outcome’ and personal or external environmental factors as ‘exposures’. The terms factors or variables were used instead of exposure because some factors (variables) were inherited traits, personal beliefs or perceptions.

The reason for conducting a case-control study was because of the low prevalence of eligible cases. Given those aged 50 to 64 years constituted 22% of the population and 8.5% of them had received influenza vaccination in 2012/13, less than 2% of people living in the region were eligible cases. The difficulty of recruiting cases doubled with an estimated response rate of 50%. A case-to-control ratio of 1:2 was chosen after some consideration of the time, cost and manpower available.

A street intercept interview method enabled the interviewers to screen and approach a larger number of people, according to their physical appearance of age. Street intercept interview also lowered the rejection rate and enabled a greater control in completing the questionnaire. It was estimated that a large number of people had to be approached should a telephone or postage survey have been used.

Cases and controls subgroups

Cases consisted of three different subtypes – those received two vaccines in 2013/12 and 2012/11 and those received one vaccine in either 2013/12 or 2012/11. Some controls had received influenza vaccine(s) before 1 September 2011. They were classified as control because:

- People aged 50 to 64 years were not recommended target group for influenza vaccination by the government before vaccination season 2011/12 (i.e., before 1 September 2011)

- It was unclear when the control had received the influenza vaccine, although it was certain they had not received the vaccine for at least two years.

Response rate

The response rate, which is the number of successfully completed interviews (numerator) divided by the number of unsuccessful interviews (denominator), was 41.7%. This low response rate was mainly due to the difficulty in finding cases because of the low vaccine coverage rate. The interviews were conducted in summer time when the street temperature was $>30^{\circ}\text{C}$ and crowded, and no incentive was offered to the respondents. The interviewers approached those who looked to be 50 to 64 year-old on the street. The person was counted as an unsuccessful interview (denominator) if s/he:

- Was 50 to 64 year-old but refused to participate; and
- Was unvaccinated in previous two years (at a stage when too many controls were interviewed); or
- Had language or communication difficulty; or
- Claimed to have completed the same survey recently.

Result

There are multi-dimensional factors that might have contributed to people's choice of whether or not to receive vaccination. These factors comprise of social, environmental and economic dynamics in a context. The factors were put in a multinomial logistic regression model and statistically adjusted for age, employment status, receiving social security, and all independent variables. Before statistical adjustment, most of these factors had statistically significant crude odds ratios. The variables affected each other and many became non-significant after adjustment. There would be a confounding effect between variables.

The majority (89%) of all the respondents were not aware that they were in a group recommended by the health authority to receive influenza vaccination. Amongst the controls, a higher percentage (71%) deemed vaccination to be 'unnecessary'. This revealed a failure of DH and health professionals in communicating the message that 'vaccination is recommended' to this age group. Given that there was an association between 'knowing oneself to be in the

recommended group for flu vaccine' and vaccination, a better communication of the risks might have improved the vaccination rate. Health promotion strategy on empowerment and enhancement of knowledge on this issue has to be planned and supported by health-care policy.

Studies suggested that previous influenza vaccination was a predictor for subsequent vaccination (OR 1.62-5.40).³⁴⁻³⁷ However, past behaviour does not provide an insight into the reasons why a person chose to be vaccinated.

Vaccination coverage rate is price sensitive. This was demonstrated in this study and in countries which provided vaccine reimbursements to users.^{38, 39} To receive influenza vaccination, most (95%) people aged 50 to 64 years in Hong Kong had to pay out-of-pocket. The odd of cases being 'eligible for free government vaccine' was 6.4 times the controls. Amongst the cases, half (52%) of them attended a private clinic or hospitals and paid the vaccination fee out-of-pocket. The majority (84%) of all respondents were willing to receive the vaccine if it was free or at a price lower than US\$6. All these associations indicated a free or subsidised vaccination service could possibly increase the vaccination rate.

There was only a mild association between chronic disease(s) and vaccination and the association was insignificant after the OR was adjusted (OR1.13, 95% CI 0.65-1.96, p=0.67). This result is in contradiction to findings in many studies indicating that the presence of chronic diseases was one of the most persistent factors associated with vaccination.^{2, 34, 35, 40-44}

'Accept advice by health professional' was moderately associated with vaccination (OR2.67, 95% CI 1.19-5.99, p=0.02). Several other studies have shown that doctors' and health professions' advice was associated with influenza vaccination.^{32, 45} Health professionals had a duty to recommend vaccination to high-risk groups in order to protect them from influenza and severe complications.

'Had family member received flu vaccine' was associated with people's uptake of the vaccination, but 'accept advice from relatives and friends' was not. In Japan, advice from health professionals, family and/or close friends were strongly

associated.³² In the USA and some other western countries, advice from family and/or close friends was not a significant factor in acceptance of influenza vaccination.^{46, 47} This could possibly be due to the differences in cultural background between individuals in these countries.

This study showed no association between vaccination with smoking and drinking. It is uncertain whether people were consistent in their health behaviours. Studies have proven that smoking is not associated with vaccination.^{36, 48} No data was found on other health behaviours such as drinking or frequent exercise, having a link to vaccination.

Given past experiences of infectious disease epidemics in Hong Kong, people may be more inclined to receive vaccination to protect themselves in anticipation of the occurrence of a disease epidemic such as SARS or swine influenza.

Previous research has suggested that newly issued recommendations are not quickly embraced by the majority of citizens. In the US, government National Health Interview Survey data did not show a marked increase in vaccination rates amongst adults aged 19 to 49 and 50 to 64, after the US Advisory Committee on Immunization Practices expanded its recommendations to these subgroups in 2000 and 2010 respectively.^{45, 49}

Strengths and limitations

A case-control study design enabled measurement of many different exposures at once and for the combined effects of exposures to be examined. In addition, data was collected within a short time-frame. Limitation of a case-control includes the information and recall bias of the respondents; difficulty in establishing a temporal or sequence of the factors and the outcomes; and the inability to estimate the coverage of vaccination in this age band. It may also be impossible to establish the timeline of events; for example, it is uncertain whether knowledge was the cause or consequence of a person who did not receive an influenza vaccine.

A limitation of using street-intercept selection bias would be the interviewers approached those who looked 50 to 64 years and potentially could miss out a

number of very young and over-aged looking individual, and the extent of this bias is difficult to assess. A test on this during the pilot phase could have provided an estimate on the degree of misses. Another bias would be due to sampling of respondents from different locations, e.g. in public and private estates, in train stations and shopping malls. A comparison of the demographic characteristics of the samples collected in different locations, and to those of the relevant population, would be useful to identify potential bias.

Further studies

Sub-group analysis of respondents was performed. These included analysis of different age bands (50-54, 55-59 and 60-64) and respondents with or without previous vaccination history. These findings were presented elsewhere.

Individual health behaviour is influenced by multifactorial factors comprised of social, environmental and economic dynamics in a given context. Studies on local vaccination policy and the views of health professionals would provide a comprehensive account of the low vaccination coverage in this age group.

Conclusion

Factors related to the existing health-care service and advice from health professionals, relatives and friends, had a comparatively strong association with influenza vaccination uptake amongst 50 to 64 year-olds, compared to other factors.

Competing Interests

The authors declare that no competing interests exist.

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Table 1. Demography of the cases and controls

		Case (n=193)		Control (n=411)		Chi-square p-value	Crude Odd Ratio (OR)			
		No.	%	No.	%		OR	95% CI		p-value
Average age (years) ± SD		57.3 ± 4.8		56.3 ± 4.4			-	-		-
Sex	Male	73	37.8	159	38.7	0.84	0.96	0.68	1.37	0.84
	Female	120	62.2	252	61.3		1.04	0.73	1.48	0.84
Age group	50 - 54	59	30.6	176	42.8	0.01	ref	ref		ref
	55 - 59	63	32.6	119	29.0		1.58	1.03	2.41	0.04
	60 - 64	71	36.8	116	28.2		1.83	1.20	2.77	0.005
Ethnic Origin	Chinese	193	100.0	410	99.8	0.49	-	-		-
Education Level	Primary or below	58	30.1	110	26.8	0.69	ref	ref		ref
	Secondary	120	62.2	260	63.9		0.88	0.60	1.29	0.50
	Tertiary or above	15	7.8	37	9.1		0.77	0.39	1.52	0.46
Occupation	Self-employed / Managing executives	1	0.37	4	1.0	0.14	-	-		-
	Professionals	11	5.7	22	5.4		-	-		-
	Clerical	22	11.4	61	14.8		-	-		-
	Servicing & retailing	33	17.1	68	16.5		-	-		-
	Technical / Nontechnical workers	11	5.7	37	9.0		-	-		-
	Unemployed	11	5.7	32	7.8		-	-		-
	Retired	52	26.9	69	16.8		-	-		-
	Housewife	47	24.4	112	27.3		-	-		-
Employed	Yes	83	43.0	198	48.2	0.27	0.82	0.58	1.15	0.24
	No	110	57.0	213	51.8		-	-		-
Health Professionals	Yes	9	4.7	6	1.5	0.02	3.30	1.16	9.41	0.03
	No	184	95.3	405	98.5		-	-		-
CSSA recipient	Yes	11	5.7	9	2.2	0.03	2.70	1.10	6.63	0.03
	No	182	94.3	402	97.8		-	-		-
Personal Monthly Income (HKD\$)	No income	105	54.7	206	50.4	0.79	ref	ref		ref
	9999 or below	29	15.2	59	14.4		0.96	0.58	1.59	0.89
	10000 - 19999	48	25.0	111	27.2		0.85	0.56	1.28	0.44
	20000 or above	10	5.2	33	8.0		0.59	0.28	1.25	0.17
Current smoker	Yes	16	8.3	20	4.9	0.10	1.77	0.89	3.49	0.11
	No	177	91.7	391	95.1		-	-		-
Current drinker	Yes	34	17.6	80	19.5	0.59	0.88	0.57	1.38	0.59
	No	159	82.4	331	80.5		-	-		-

Table 2. Comparing study variables between cases and controls by crude odds ratio and multinomial logistic regression analysis

	Cases (193)		Control (411)		Odd Ratio (Crude)			Odd Ratio (Adjusted)				
	Count	%	Count	%	value	95% CI	p-value	value	95% CI	p-value		
Knowledge												
Knowing oneself to be in the recommended group for flu vaccine	37	19.6	25	6.1	3.75	2.18	6.44	0.002	2.34	1.23	4.44	0.01
Knowing flu vaccine provides 70-90% protection in healthy adults	89	46.6	140	34.1	1.66	1.17	2.35	0.005	1.86	1.12	3.10	0.02
Knowing about the Government Vaccination Programme	128	68.0	219	53.5	1.79	1.25	2.57	0.001	1.09	0.68	1.75	0.72
Knowing flu vaccine reduces flu complications and related hospitalisation	180	97.8	366	93.4	3.20	1.10	9.30	0.02	0.89	0.25	3.19	0.86
Needs												
Live with children < 6 years or elderly >65 years	53	27.5	85	20.7	1.45	0.98	2.16	0.033	1.23	0.74	2.04	0.43
Presence of chronic disease(s)	78	40.4	111	27.1	1.83	1.27	2.62	<0.001	1.13	0.65	1.96	0.67
Visited doctors in the past 3 months	92	47.7	141	34.3	1.74	1.23	2.47	0.002	1.12	0.67	1.87	0.68
Behaviour												
Current smoker	16	8.3	20	4.9	1.77	0.89	3.49	0.11	0.72	0.27	1.92	0.52
Current drinker	34	17.6	80	19.5	0.88	0.57	1.38	0.59	-	-	-	-
Belief & perception												
Perceived having severe or moderate symptoms when contracting flu	17	8.8	15	3.6	2.55	1.25	5.22	<0.001	2.90	1.21	6.97	0.02
Perceived flu vaccine to be safe	183	98.4	342	89.8	6.96	2.12	22.82	<0.001	3.99	0.78	20.41	0.10
Believed flu vaccine has additional benefits other than flu protection	181	93.8	356	87.3	2.20	1.15	4.23	0.013	1.36	0.58	3.21	0.48
Perceived very high and high chance of contracting flu in the next 12 months	55	31.1	77	19.9	1.81	1.21	2.72	0.004	1.03	0.61	1.76	0.90
Perception of having very good or good health	105	54.4	281	68.4	0.55	0.39	0.78	<0.001	0.72	0.44	1.19	0.20
Perception of having severe adverse events after vaccine	22	12.2	89	24.9	0.42	0.25	0.70	<0.001	0.64	0.33	1.22	0.18
Belief in very good or good vaccine efficacy	147	76.2	269	65.5	1.69	1.14	2.49	0.007	0.62	0.36	1.08	0.09
Health-care system												
Eligible for free government vaccine	45	23.6	21	5.1	5.71	3.29	9.91	<0.001	6.38	3.43	11.87	<0.001
Willing to receive flu vaccination for free	184	95.8	309	75.7	7.37	3.50	15.49	<0.001	4.84	2.13	11.03	<0.001
Convenient to reach a vaccination location	187	96.9	370	90.0	3.45	1.44	8.28	0.002	2.87	1.06	7.74	0.04
Prefer public clinic for injection	105	54.7	291	71.0	0.48	0.33	0.68	<0.001	0.35	0.22	0.55	<0.001
Will respond to Government telephone reminder service on flu shot	105	54.4	160	39.6	1.82	1.29	2.57	<0.001	0.84	0.51	1.38	0.49
Advice												
Accept advice from health professionals	183	94.8	333	81.2	4.23	2.14	8.38	<0.001	2.67	1.19	5.99	0.02
Had family member receive flu vaccine	76	41.8	74	18.3	3.20	2.17	4.71	<0.001	2.47	1.54	3.95	<0.001
Accept advice from relatives and friends	86	44.8	101	24.6	2.48	1.73	3.57	<0.001	1.47	0.84	2.56	0.18
External factors												
Will receive flu vaccine when there is an epidemic	181	94.8	327	81.3	4.15	2.09	8.23	<0.001	2.40	1.07	5.37	0.03

Table 3. Responses of cases and controls in multiple answer questions

		Cases (n=191)		Control (n=413)		Pearson Chi-Square Tests		
		Count	Column %	Count	Column %	Chi-square	df	Sig.
Flu vaccine history	Received on 2010/11 and/ or 2011/12	191	27.8	-	-	-	-	-
	Last dose received > 2 years	-	-	106	25.6	-	-	-
	Never	-	-	308	74.4	-	-	-
Reason for receiving vaccine	Advice from health professionals	91	47.2	64	61.0	11.56	8	0.17
	Perceive unsatisfactory health	45	23.3	19	18.1			
	Belong to high-risk group	8	4.1	2	1.9			
	Perceived vaccine	87	45.1	48	45.7			
	Required by work	21	10.9	13	12.4			
	Free vaccine	18	9.3	4	3.8			
	Protect family members	48	24.9	25	23.8			
	Others	5	2.6	5	4.8			
Location received vaccine	Public clinic	94	48.7	62	15.0	5.41	4	0.25
	Private clinic	83	43.0	36	34.3			
	Hospital	8	4.1	3	2.9			
	Others	10	5.2	5	4.8			
Preferred location for receiving vaccine	Public clinic	105	54.7	291	71.0	28.07	4	<0.001
	Private clinic	85	44.3	127	31.0			
	Hospital	7	3.6	21	5.1			
	Others	0	0.0	0	0.0			
Other benefits for receiving vaccine	Protect Family Members	176	91.2	347	85.0	10.33	3	0.16
	Working Necessity	13	6.7	25	6.1			
	Other Reasons	0	0.0	0	0.0			
	No	12	6.2	52	12.7			
Medical consultation	Consult Doctors	80	87.0	132	93.6	4.82	2	0.09
	Consult Chinese Doctors	31	33.7	36	25.5			
Reasons for NOT receiving vaccine	Unnecessary	-	-	216	70.8	-	-	-
	Non-high risk group	-	-	113	37.0			
	Busy	-	-	78	25.6			
	Side effects of vaccine	-	-	58	19.0			
	Flu is a mild illness	-	-	19	6.2			
	Expensive	-	-	16	5.2			
	Do not know where to get vaccine	-	-	14	4.6			
	Vaccine is ineffective	-	-	12	3.9			

* All questions, except the first, allow for the selection of more than one choice of answer.

5.2 Supplementary research result and discussion

5.2.1. Subgroup analysis

A subgroup analysis had been conducted where the participants were divided into three age groups: 50 to 54, 55 to 59 and 60 to 64. In each subgroup, cases were compared to controls. There was an increasing trend of vaccination in the 55 to 59 group (OR1.58, 95% CI 1.03-2.41, $p=0.04$) and 60 to 64 group (OR1.83, 95% CI 1.20-2.77, $p=0.005$) when compared to the 50 to 54 group. Here I explore if there is an increasing trend in association with the 38 variables across the three age groups.

There is no increasing or decreasing trend observed in any of the variables. 'Eligible for free government vaccine' (OR from 7.72 to 14.83) and 'willing to receive flu vaccination for free' (OR from 8.04 to 11.46) were factors strongly associated with vaccination. 'Preferred public clinic for injection' (OR from 0.21 to 0.24) and 'perception of having severe adverse events after vaccine' (OR0.29, 95% CI 0.09-0.97, $p=0.04$) were strongly negatively associated with vaccination. This means more cases (vaccinated individuals) did not choose to vaccinate at a public clinic. More controls (unvaccinated individuals) had a negative perception of vaccination to have adverse events. Most variables were found to be statistically significant for one age group only. All the statistically significant ORs were presented in Table 9.

Interpretation

There is no gradation in the degree of association of variables with age. One possible reason for this is insufficient power to detect the small effect size due to small sample size. The sample size for each subgroup is around 200, so the effect size could be detected given a moderate degree of prevalence in the exposed (e.g., >20%). It appears that there is no real trend of association between vaccination and the variables under study.

Table 9 Comparing study variables between cases and controls by adjusted odds ratio for different age groups

Factors	50-54				55-59				60-64			
	Cases (n=59)		Control (n=176)		Cases (n=63)		Control (n=119)		Cases (n=71)		Control (n=116)	
	p value	Odds ratio (adjusted)			p value	Odds ratio (adjusted)			p value	Odds ratio (adjusted)		
	Value	95% CI		Value	95% CI		Value	95% CI		Value	95% CI	
Knowing oneself to be in the recommended group for flu vaccine	-	-	-	-	-	-	-	-	0.03	3.40	1.14	10.19
Knowing flu vaccine provides 70-90% protection in healthy adults	-	-	-	-	-	-	-	-	0.04	2.39	1.06	5.40
Perceived having severe or moderate symptoms when contracting flu	0.02	5.528	1.36	22.55	-	-	-	-	-	-	-	-
Perception of having severe adverse events after vaccine	0.04	0.29	0.09	0.97	-	-	-	-	-	-	-	-
Belief in very good or good vaccine efficacy	-	-	-	-	-	-	-	-	0.01	3.83	1.41	10.41
Eligible for free government vaccine	0.02	14.83	1.43	153.67	-	-	-	-	<.0001	7.72	3.07	19.45
Willing to receive flu vaccination for free	0.01	8.04	1.60	40.34	<0.001	11.46	2.99	43.99	-	-	-	-
Preferred public clinic for injection	<0.001	0.24	0.12	0.51	0.01	0.21	0.07	0.64	-	-	-	-
Accept advice from health professionals	-	-	-	-	-	-	-	-	0.02	14.12	1.53	130.64
Accept advice from relatives and friends	-	-	-	-	<0.001	3.86	1.81	8.19	-	-	-	-
Had family member receive flu vaccine	0.02	2.431	1.12	5.28	-	-	-	-	0.03	2.71	1.12	6.51

* Variables with statistically insignificant adjusted OR are not shown

5.2.2. Strengths and limitations of the case-control study

This case-control study assesses multiple causes relating to one outcome event. It is a suitable method for assessing the causes of a new problem with rare outcome. This study design proves associations but does not demonstrate causation.¹⁵⁴ It intended to establish and quantify associations by comparing the odds of the exposures in the cases and controls, i.e., the odds ratios. It is retrospective so can assess outcomes that happened in the past. The data collection period was finished within 2 months, which is relatively short when compared to a cohort study.

The problem of recall bias could be less serious because the cases and controls were asked about their vaccination status and related information in recent two years. Their answers on demography, knowledge, belief and perceptions, and other parameters may not have changed a lot within these two years. Besides, the views they had were what they hold true, and it could not be said as biased or wrong. So in the study hypothesis, the cases were expected to have different views, beliefs and perceptions from the controls. There could give incomplete or deliberately inaccurate answers, but it is difficult to validate the answer of a respondent. Interviewers and interviewees were not blinded during interviews. There would be interviewer bias if the interviewer had strong and different presumptions about the cases and the controls. This led to inconsistency in questioning, sending non-verbal cues or placing emphasis on interpreting answers.¹⁵⁵ There was a risk for the interviewees of consciously or subconsciously affecting their answers.

Table 10 Strengths and limitations of the case-control study

Strengths	Limitations
◆ Suitable for rare outcome (8.5% among adults aged 50 to 64)	◆ Difficult in finding control to match with cases
◆ Allow examination of multiple exposures or risk factors	◆ Established association between exposures and outcome, not causation
◆ Good for examining past outcomes (vaccination within 2 years)	◆ Susceptible to recall and information bias
◆ Obtained result within a short time (2 months)	◆ Difficult to validate the information obtained
◆ Interviewers clarified questions; and ensure questionnaire was completed	◆ Interviewers and interviewees were not blinded

5.2.3. Internal validity

To assess the degree of internal validity, an adopted methodology checklist on case-control studies from UK National Institute for Health and Care Excellence (NICE) was used.¹⁵⁶ Out of the 11 questions, 7 were well covered by the case-control study. There were inadequacy in identifying the similarities or differences between the participants (respondents) and non-participants (non-respondents). The response rate is on the low side and without separate figures for the cases and controls.

Table 11 Internal validity checklist on the case-control study

General		
1.1	The study addresses an appropriate and clearly focused question	Well covered, in section 4.1
Selection of Subjects		
1.2	The cases and controls are taken from comparable populations	Well covered, in section 4.3
1.3	The same exclusion criteria are used for both cases and controls	Well covered, in section 5.1
1.4	What percentage of each group (cases and controls) participated in the study?	Overall response rate 41.7%
1.5	Participants and non-participants are compared to establish their similarities or differences	Poorly addressed
1.6	Cases are clearly defined and differentiated from controls	Well covered, in section 5.1
1.7	It is clearly established that controls are non-cases	Well covered, in section 5.1
Assessment		
1.8	Measures were taken to prevent knowledge of primary exposure from influencing case ascertainment	Not applicable
1.9	Exposure status is measured in a standard, valid and reliable way	Well covered, in section 4.4
Confounding		
1.10	The main potential confounders are identified and taken into account in the design and analysis	Adequately addressed
Statistical analysis		
1.11	Confidence intervals are provided	Well covered, in section 5.1

5.2.4. External validity – generalisation of research findings

Provided the internal validity of the case-control study is accepted, I would choose to how applicable the findings are to the target population, or to relevant populations in other parts of the world. First, I would consider the representativeness of the sampled population. Based on the detailed selection of the sampling districts, choice of suitable recruitment time, and comparable demography of the samples (cases and controls) with the population, I accept that the samples could represent the general population of people aged 50 to 64 in Hong Kong. Second, I would examine the randomness of the non-respondents because reason for losses due to non-participation could be related to the exposure or to the outcome.¹⁵⁷ Given the limitations of the street-intercept interview method, it is difficult to solicit views from non-respondents because they just walked away. The overall response rate of 41.7% in this study was disappointing, but survey research literature reveals that response rates in intercept studies seldom exceed 50%.¹⁵⁸ It was assuring that most finished questionnaires were completed satisfactorily, with a completion rate of 98%.

Thus I conclude that the findings of the case-control study could be generalised to the general population aged 50 to 64 in Hong Kong. However, I have reservations in applying the results to other relevant populations. This is based on my general knowledge of differences between cultures, beliefs and norms; and also differences in the external environment, such as health systems and service provision.

5.2.5. Study improvements

The case-control study could have been improved if a matched-case control study was performed. Each case could be matched with a control from the same age, sex, place of residence, or socio-economic status. However, the matched parameters (e.g., age or sex) cannot be examined in the study. There would also be a substantial increase in time and cost in recruiting and matching eligible control participants. Yet, matching could eliminate the influence of known and unknown confounding factors that are difficult to measure.¹⁵⁹

The questionnaire could have been better designed by enhancing conceptualisation with a prior focus group discussion, and by establishing reliability with additional statistical tests. Instead, the conceptualisation and content of the questionnaire was formed through literature review. The questionnaire's reliability could have been improved if a double interview was performed for each interviewee during pilot. Then statistical reliability tests such as test-retest reliability coefficients and Pearson's correlation could be calculated during questionnaire development. A double interview would be more plausible if the interviews were conducted in a clinic or centre setting than in the street.

During sampling, in addition to keeping a pen and paper record, it would have been better if all interviews were audio-taped for cross checking and audit purposes. For a study with a larger budget, a note pad could be used so that direct input of data into the relevant field could save subsequent input effort. Besides, pictures and animations could be used to arouse participants' interest.

The response rate of the case-control study was 41.7%. To improve response rate, some proven effective measures had been considered: giving incentives such as gift or cash coupon; and distributing attractive questionnaires on colour paper with appealing look.^{160,161,162} These were not implemented because the response rate during the pilot phase was around the expected average response rate of surveys of 55%¹⁴⁴, and that the questionnaires were filled by the interviewers.

Other subgroup analyses could have been performed if time allowed. Clearly there might be differences in subgroups with or without chronic disease(s); working and unemployed; receiving social assistance and those who were not; those ever vaccinated and those never vaccinated. Identifying an increasing or decreasing trend in OR could help to establish dose-response relationships and suggest causations. Possible problems are small sample size in some subgroups, e.g., there were only 20 social assistance recipients. Interpretations of significant OR should err on the side of caution because sometimes 'data dredging' or 'data fishing' can, by chance, uncover unexpected associations.

6. Discussion and Recommendation

This chapter is an overview of the thesis as a whole, and contains a discussion of the results of all the chapters. It also points out the implications of the findings on health service and policy, suggests potential areas for future research, and details the dissemination plan of the research findings.

6.1 Concluding remarks

6.1.1. Achieving research objectives

In the introduction of this thesis, I identified three research objectives and I achieved these using three different study methods. First, I assessed the health needs for influenza vaccination in people aged 50 to 64 in Hong Kong, using epidemiological, comparative and corporate approaches. This served to provide background information on understanding the broader context of my research, and deepened my knowledge on what is known about this topic. Second, I examined the factors associated with the uptake of seasonal influenza vaccination in adults aged 18 to 64 years old through systematic literature review. The reviewed information on factors (variables) associated with the uptake of influenza vaccination was essential in formulating the content of the case-control study questionnaire. Lastly, I conducted a case-control study to determine which factors (variables) were associated with influenza vaccine uptake in residents of Hong Kong aged 50 to 64 years. The result provides new data and insight which will serve as a reference for influenza vaccination services.

6.1.2. Original contribution

This work provides new data and understanding of the factors affecting vaccination amongst middle-aged adults. The case-control study quantifies factors associated with the uptake of influenza vaccine more precisely with regard to the 50 to 64 age group. It enhances understanding of vaccination behaviour by providing the latest information. Since many places have not included this age group in their national vaccination programmes, the result should guide health workers planning influenza vaccination services and strategies for middle-aged healthy adults.

6.1.3. Scope of the thesis

Individual health behaviour is influenced by multifactorial factors which are interactions of ‘socioeconomic and political context’, ‘individual’s structural determinants’, and ‘intermediary determinants of health’.^{163,164} Given the breadth of the thesis’s scope, its focus and case-control study is concerned with the latter two. The most important ‘individual’s structural determinants’ proxy indicators are income, education, occupation, social class, gender, and race/ethnicity. The main categories of ‘intermediary determinants of health’ are material circumstances; psychosocial circumstances; behavioural and/or biological factors; and the health system.

What is not included in the thesis and the case-control study belongs to the ‘socioeconomic and political context’ of influenza vaccination. These are the governance, health and social policy, cultural norms and societal values.¹⁶³ In addition, the health implementation, equity and stakeholders’ role (e.g., health professionals, vaccine industry) have not been addressed.

6.1.4. Conceptual framework and health behaviour theories

A conceptual framework explains, either graphically or in narrative form, the main things to be studied – the key factors, constructs or variables – and the presumed relationships among them.¹⁶⁵ A framework is not explicitly described in this thesis because the understanding is sufficient and clear without citing theories, using concepts and drawing diagrams. A conceptual framework diagram was constructed for this thesis, but I decided not to include it because I felt readers could understand the thesis equally well, if not better, without the diagram.

Although no theories were mentioned, framework, theories and models explaining and predicting health behaviours were studied during the course of the research design. These theories have been extremely influential in conceptualising, predicting and changing health behaviour.¹⁶⁶ One of the earliest models is the Health Belief Model which explains differential behaviour in utilisation of prevention programmes such as immunisation.¹⁶⁷ Other health promotion theories and models such as Theory of Reasoned Action¹⁶⁸, Theory of Planned

Behaviour¹⁶⁹ and The Social Learning Theory were studied. These theories cite environmental, personal, and behavioural characteristics as the major factors in behavioural determination. Understanding these theories can help to define the scope of the research and acknowledge what is and is not included in the thesis to explain vaccine uptake behaviour.

6.1.5. Comparing results of the systematic literature review and the case-control study

The result of the case-control study is compared with the systematic literature review. By doing this, I compared factors associated with vaccination uptake in people aged 18 to 64 living in different parts of the world, with those aged 50 to 64 living in Hong Kong. While the presence of chronic disease(s) is one of the consistent factors with high OR in many studies, it was not a significant factor in the local study group. Free vaccination, ‘accept advice from health professionals’ and cues to action (‘had family member receive flu vaccine’), were consistently associated with vaccination in both the review and the case-control study. ‘Convenient to reach a vaccination location’ and ‘will receive flu vaccine when there is an epidemic’ were two associated factors which were not commonly mentioned in studies done in other parts of the world.

Table 12 Comparing factors with high odds ratios (OR) in the systematic literature review and the case-control study

Systematic literature review	OR	Case-control study	OR
Presence of chronic disease(s)	1.38-13.7	Eligible for free government vaccine	6.38
Advice from health professionals	1.23-13.0	Willing to receive flu vaccination for free	4.84
Perceived vaccine efficacy	2.7-10.55	Perceived having severe or moderate symptoms when contracting flu	2.90
Advice from doctors	4.03-7.82	Convenient to reach a vaccination location	2.87
Free vaccination	4.5-7.8	Accept advice from health professionals	2.67
Cues to action (relative and friends receive vaccine)	6.44	Had family member receive flu vaccine	2.47
Perceived chances of contracting influenza	1.62-5.40	Will receive flu vaccine when there is an epidemic	2.40

*‘Age’ with OR 1.06-23.7 was not included because subjects in the case-control study were all 50 to 64 years; ‘advice from family and/or close friends’ with OR=17.74 is not included because of estimated cultural bias

6.1.6. Controversies of influenza vaccination

Some recent studies have questioned the benefit of influenza vaccine efficacy. A Cochrane review concluded that the vaccine had modest effects in reducing working days lost, but had no effect on reducing hospital admissions or complication rates in healthy adults.⁹¹ Two other reviews stated there was a lack of evidence on protection of vaccine in adults aged 65 years or older.^{80,170} Later there was another study on a reanalysis of one of these reviews and concluded in favour of vaccination in the elderly population.¹⁷¹

Till now, experts generally agree that vaccination is the first line of defence for reducing influenza morbidity and mortality.⁷² Influenza vaccine would continue to be used by health authorities to protect high-risk people from influenza related complications. Revision of vaccination policy and service is an on-going task for health authorities wishing to maximize influenza epidemic and pandemic preparedness.

6.2 Informing policy

6.2.1. Argument on health inequality and health inequity

The policy decision to limit the government vaccination service to those receiving CSSA^{§§§§} and having chronic diseases amongst 50 to 64 year-olds has caused major concern and stimulated discussion. Most (95%) of this group recommended by DH to receive influenza vaccine had to pay out-of-pocket if they choose to be vaccinated. Firstly, this decision may fail to meet public expectations, as people may have expected that all the groups recommended for vaccination by the DH would enjoy free or subsidized vaccination services. Secondly, it raised issues around equality and led to people arguing why free service was limited to CSSA recipients only. Thirdly, the differences in vaccination service provisions to the different recommended target groups have caused confusion in health promotion.

The advantage of this decision was that only a small amount of additional funding was incurred, and therefore this additional budget did not require approval from the Legislative Council – which saved a lot of time. The moderately increased workload and budget could easily be absorbed by the existing service provision in the public sector. This service expansion minimized competition with other health priorities for resources.

Although the price of receiving an influenza vaccination constitute <3.5% of a monthly income, this does not necessarily mean socio-economically deprived groups who are ineligible for free vaccination would be willing to pay for the vaccine. Subsidised vaccination would attract those who are willing to pay for a discounted price, and these people may be among ‘the better off’ – those who have easier access to vaccination services, who are better informed about the availability and effectiveness of the vaccine, who work less demanding working hours, etc. The inverse care law, first described by Julian Tudor Hart in 1971, states that the availability of good medical care tends to vary inversely with the need for it in the population served.¹⁷²

^{§§§§} CSSA Scheme is a social safety net for those who cannot support themselves financially. It is designed to bring their income up to a prescribed level to meet their basic needs.

To tackle this inequity, there is a need to find ways to diminish the vaccination barriers and/or enhance protection by herd immunity. Hong Kong has the highest income disparity in Asia (Gini coefficient 0.537 in 2011) and the government has started to put forward poverty alleviation policies in recent years.^{173, 174} Free influenza vaccination or special healthcare allowance could be included as part of the package to support those below the poverty line. Indirect protection (herd immunity) can be achieved by selectively vaccinating groups that are important in transmission, such as young children living in families below the poverty line. However, the low vaccination rate in the population and amongst the high-risk group (8.4% for children under 5 and 39.1% for elders over 65), plus a high mobility of city people, renders achieving herd immunity a challenging prospect.⁹

6.2.2. Evidence-based recommendations on policy change

Recommendation 1: The provision of free or subsidized vaccine for people age 50 to 64 years could probably improve the coverage rate.

The case-control study evidenced that the most important barrier to influenza vaccination as being financial. Any policy initiative to increase vaccine uptake will need to address the financial barrier. The first and second most strongly associated factors with vaccinations both related to financial incentives – ‘eligible for free government vaccine’ (OR6.38) and ‘willing to receive flu vaccination for free’ (OR 4.84). This was further supported by the systematic review of a strong association of free vaccine and vaccination (OR7.8). In addition, study on the influenza vaccine provision in 157 countries found policy measures that directly impact on patients (i.e., money reimbursement and communication) were highly correlated with higher vaccine dose distribution rate in the population, irrespective of a country’s development status.¹⁸

An alternative would be to provide a subsidy or repayment for the vaccine. In the case-control study, one in four (24.7%) of the cases and controls were willing to receive the vaccine if it cost below HKD\$50 (USD\$6.4), and an additional 12.1% was willing to pay if it cost below HKD\$100 (USD\$12.8). The median cost of one

dose of influenza vaccine, including the cost of the vaccines and consultation fees was \$180 (USD\$23).¹⁰⁴ A subsidy of \$130(USD\$16.6) could lead to a substantial increase in people’s willingness to receive influenza vaccination, especially amongst those that have not been vaccinated (controls) in 2011/12 and 2012/13.

Table 13 Amount willing to pay for influenza vaccine in the case-control study

Amount willing to pay	Case	%	Control	%	Total	Total %
\$0	108	56.0%	250	60.83%	358	59.3%
< \$50	49	25.4%	100	24.33%	149	24.7%
< \$100	22	11.4%	37	9.00%	59	9.8%
<\$150	2	1.0%	9	2.19%	11	1.8%
> \$150	3	1.6%	0	0.00%	3	0.5%
Fee is not a concern	9	4.7%	15	3.65%	24	4.0%
	193		411		604	

Recommendation 2: Health promotion should address ‘the perception of having severe or moderate symptoms when contracting flu’, ‘knowledge of oneself to be in the recommended group for flu vaccine’ and ‘good vaccine protection for healthy adults’.

Even if there are restrictions on funding, resources and service provision, DH still has an obligation to explore ways to increase vaccination coverage in this newly recommended group; as well as find other measures to reduce serious influenza mortality and morbidity. If DH with continues the existing policy and receives no additional funding, health promotion could target this group and encourage out-of pocket payment. There needs to be a health promotion strategy and activities targeted at the 50 to 64 age group. Health providers could be engaged, with or without incentives, to promote the benefit of vaccination. Other measures, such as personal hygiene and healthy life style, should also be promoted to improve general health and decrease influenza related morbidity. The high affordability of an annual influenza vaccine for the general public could be the basis of success.

Recommendation 3: Review on the policy

Public health policy makers in DH should conduct a review of the impact and cost-effectiveness of this vaccine policy after it has been implemented for three years. Depending on the target coverage set by DH, they can choose whether to provide a free vaccination for this group, or just give them subsidy for injection in the private sector. The amount of money given as a subsidy affects the coverage – the larger the amount, the greater the incentive would be to the vaccine recipient and healthcare provider. The review data on vaccine impact and cost would support an appeal for additional funding by the Secretary in the Bureau and in the Legislative Council. In contrast, if the review result is unfavourable, DH may consider maintaining current service provision. DH should further consult the SCVPD to decide if adults aged 50 to 64 should remain as a recommended group.

6.3 Future research

During the research process, a significant amount of time was needed to search for relevant information on people aged 50 to 64 year or middle-aged adult. This suggested more research or data presentation on this age group would improve understanding and inform future vaccination planning. Many of the influenza vaccination studies on general populations have included this age group. For a study with a large sample size, a subgroup analysis would yield valuable information. Here, I suggest some fruitful avenues:

- Reassess if there is local health needs for people aged 50 to 64 to be included as the recommended target group for influenza vaccination in the coming year. There is constant change in the impact of influenza strains on disease mortality and morbidity.
- Explore and engage with overseas health counterparts on the reasons for not including people aged 50 to 64 in their vaccination programme. Many overseas health authorities chose not to recommend this age group for influenza vaccination despite favourable cost-effectiveness analysis.
- Examine views and practices of health professionals on recommending influenza vaccination to people aged 50 to 64. Health professionals' advice is associated with vaccination uptake their view influences the vaccination coverage.

6.4 Dissemination plan

In order to share the research findings with interested public health workers, the two research papers will be submitted to peer-reviewed journal(s). In addition to this, a summary will be written in the Hong Kong Medical Association magazine to inform local practitioners. A poster presentation on the case-control study was held in the Annual Scientific Meeting of the Hong Kong College of Community Medicine on the 22 September 2014. (Annex 3) Relevant sections of this research will be communicated to the DH Vaccination Office for policy and service improvement.

7. Integrating Statement of DrPH

7.1 Introduction

This integrating statement summarizes my learning processing since 2007 during the course of my Doctorate in Public Health (DrPH). A DrPH is a degree which combines theoretical and practical knowledge on leadership, management and research. I enrolled on this degree a few years after I finished a master's degree in public health and worked in the Department of Health as a public health physician. I decided to undertake this degree with a view to gain insight into international best practices in public health policy, leadership skills and the application of evidence-based medicine.

The DrPH consists of three components, structured chronologically: the taught courses, the Organisational and Policy Analysis (OPA) and the research project. Taught courses took place between late 2007 and early 2008, the OPA attachment from June to November 2010 and the research project since 2012. I began this degree as full-time student in September 2007, temporarily stopped for half year in 2009, and resumed part-time at the end of the same year.

Figure 6 Timeline of the DrPH study



7.2 Taught courses

The taught components consisted of compulsory and selected modules. The core compulsory modules in the first term during the first year covered two subject areas: leadership, management and development (LMD); and evidence-based public health practice (EBPHP). I also attended four selected modules; three were done in 2008 before the OPA attachment and one in 2013.

The compulsory modules were exclusive to DrPH students. In 2007/08 there were around 10 students enrolled, each from a different country in Africa, America, Asia, or Europe. All of us had experience in supporting or managing public health programmes in Government and/or NGOs. Taking advantage of this experience, we often discussed the similarities and differences in public health policies, practices and decision-making process in related to local cultures, resources and constrains. We shared our views on important public health issues such as health finance systems, maternal and child health, HIV/AIDS, TB, Accident and Emergency Department (AED) services, etc.

The LMD module teaching sessions introduced major organisation and behaviour theories and their application. The most memorable part of this course was the three day personal development retreat. The retreat enabled me to reflect upon my personality, personal management and leadership styles. We spent more than a half day interpreting and sharing results of the Myers-Briggs personality test. I had a heated discussion with the coordinator and my classmates because I disagreed with the personality test result and claimed it not reflect my true personality. Several years later, however after holding a managerial position, I realized that the test result did reveal some of my core strengths and weaknesses in leadership and management.

The EBPHP modules introduced the fundamental concept of evidence-based policy theory and research methods in public health practice. This course taught me to better locate, assess, collate, present, and use the research-based information to guide public health policy and practices. These are essential skills for the literature review in the OPA, research project and my work on policy decision at the DH.

For the four selective modules, three were done in 2008 before the OPA attachment and one in 2013. In 2008, I selected modules on health impact and decision analysis, health-care evaluation, and financial management. These modules better equipped me for the OPA attachment. During the writing-up phase of the research project in 2013, I attended one more module on extended

epidemiology, to cover particular skills that were required for data analysis and discussion in the research project.

7.3 Organisational and Policy Analysis (OPA)

The OPA attachment was undertaken over a 6 month period from June 2010 in a small-scale NGO, called Community Health Organisation for Intervention, Care and Empowerment (CHOICE), in Hong Kong, China. The analysis, writing and revision of the OPA report lasted another 12 months. My attachment was undertaken outside my normal place of work as a volunteer.

It took me some effort to identify an organisation which would allow me attach myself to them, interview their staff, evaluate their work, and write about it. I was working in DH but an OPA attachment there was impossible because of restrictions on disclosing internal practices and information, let alone being able to analyse and critique it. Besides, the DH service had a recent internal evaluation and it seemed there was little I could recommend further. On the contrary, CHOICE as a small-organisation with fewer than 10 staff was eager to enrol an additional volunteer. It's Chief Executive and Board Members were enthusiastic about exploring and discussing organisational issues such as enhancing funding, improving staff motivation and service provision. By studying the operation of a small organisation, a more comprehensive view of the whole organisation was obtainable.

During OPA, I observed and analysed how CHOICE had achieved its public health goals by using semi-structured interviews, participant observation, document review, and relevant literature search. The data collected was analysed by applying various analysis frameworks and theories I learned during the taught modules. I studied the organisational structure, management and leadership, its relationships with the external environment, and how these factors impacted on the organisation. After completing the OPA attachment, I analysed the data collected and formulated a list of practical recommendations. I feedback these findings during a sharing session to CHOICE Board Members and staff, hoping

that this might encourage new ideas to emerge on enhancing the organisation's effectiveness and sustainability.

The OPA gave me an opportunity to gain a deeper understanding of how a small-scale NGOs is managed, how it functions to fill service gaps and how it acted within the policy environment. I still participated in the activity CHOICE organised several years after the OPA attachment, and maintained a good relationship with some of the staff and Board Members. One of the Board Members later became a member of the Advisory Committee for my research project.

7.4 Research project

The research project was the most challenging part of all because of the originality and scientific rigour that was required. Formulating the research topic took years because the original research topic, which I submitted on admission to the school, was dropped due to a change of work. It was not until 2011 that I managed to formulate this research topic when I worked in the DH Vaccination Office (VO). During my stay in the office I assisted with the needs assessment and planning of a proposed change in vaccination policy and it was in this context that the research topic was developed. Subsequently, the research project has taken 24 months.

I have conducted a literature review, prepared a research protocol and a plan for data collection since May 2012. The first research protocol was rejected by the review committee on November 2012 and a subsequent resubmission on July 2013 was accepted. Following the committee's approval, I proceeded to data collection and then result analysis. The first draft of research articles of the thesis was finished on January 2014. During this period, the supervisor and the advisory committee members gave ample academic support and guidance. The two M.Sc. modules, workshops and seminars I attended at the LSHTM also helped to strengthen my skills for undertaking the data analysis and discussion.

Support from the academic staff, my supervisor and, most importantly, from student peers was crucial for maintaining my positive stamina and motivation.

DrPH students usually compose 10 percent of the post-graduate research student population at LSHTM. Being in the minority, our DrPH class maintained contact and notified others classmates about each other's progress. This avoided feelings of isolation and being left behind.

In undertaking the research project, I learned to take responsibility for managing my learning process. There were people around to support, but for the research project, I had to take the initiative to do it. This has required me to conduct an exploration of how to apply the scientific methodology in finding answers to specific questions. There were also opportunities to get a feel of the academic world and engage in writing research funding proposals, project management, scientific presentations, publications, etc. This training equipped me with the ability to better critically appraise and apply research findings in public health practices.

7.5 Conclusion

The DrPH course was unique in providing a diversity of public health knowledge and skills, with emphasis on practical applications. The cultural variety and scientific excellence of the school broadened my understanding of the subject and prepared me for a leading role in my public health career.

Annex 1

50 至 64 歲香港人士接種季節性流感疫苗的因素 Factors associated with uptake of influenza vaccine in people aged 50 to 64 years in Hong Kong: a case-control study 問卷 Questionnaire

訪問員編號 Interviewer no.:

訪問日期 Date of interview:

訪問時間 (開始/完結) Time of interview (start / end):

訪問地點 Location of interview:

引言 Introduction

我們誠意邀請你參與這項由楊貝珊醫生(倫敦衛生和熱帶醫學院)執行的研究。這項目已獲得香港理工大學人類課題道德委員會和倫敦衛生和熱帶醫學院道德委員會批准。在你決定之前，請仔細閱讀以下訊息，明白研究的內容和目的。如果你想，可以與他人討論。

這項學術研究項目目的是探討 50 至 64 歲香港人士接種季節性流感疫苗的因素。這項研究結果可作有用的參考，從而協助公共衛生從業者制定合適流感疫苗注射服務和社區健康推廣宣傳的工作。調查問卷只需要約 10 分鐘的時間完成。

參與是自願的，是由你來決定是否參加。這項研究應不會對你造成任何不適。你有權隨時退出而不需要給予理由，這不會有任何後果。你所提供的個人資料是完全匿名和保密的。參與者在問卷中所採用的識別碼只有研究員知道。你有權隨時退出而不受任何懲處。如果您想查詢更多關於這項研究，歡迎在辦公時間聯絡楊貝珊醫生(電話: 97717501) 或電郵tak.fai.tong@polyu.edu.hk。

若你對此研究有任何投訴，請以書面形式去信香港理工大學，與人類課題道德屬下委員會秘書 Dr. Virginia Cheng 聯絡。(C/O香港理工大學研究事務處)，請註明這項研究的負責人及部門。

感謝您參與這項研究。

楊貝珊

項目負責人

You are invited to participate on a study conducted by Dr. YEUNG Pui Shan from the London School of Hygiene and Tropical Medicine (LSHTM). This academic research project has been approved by the Human Subjects Ethics Sub-committee (HSESC) of

The Hong Kong Polytechnic University and the LSHTM Ethics Committee. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish.

The aim of this study is to explore the factors associated with uptake of influenza vaccination in residents of Hong Kong aged 50 to 64 years. The result of this study may serve as useful reference public health workers on planning influenza vaccination service and health promotion work. The interview takes about 10 minutes to complete a questionnaire.

Participation is voluntary. It is up to you to decide whether or not to take part. This study should not cause you any discomfort. You are free to withdraw at any time without giving a reason and this will not have any consequence. All information related to you will remain anonymous and confidential, and will be identifiable by codes only known to the researcher. You have every right to withdrawn from the study before or during the measurement without penalty of any kind. If you would like to get more information about this study, please contact Dr. Yeung Pui Shan at 9771 7501 during office or via tak.fai.tong@polyu.edu.hk.

If you have any complaints about the conduct of this research study, please do not hesitate to contact Dr. Virginia Cheng, Secretary of the Human Subjects Ethics Subcommittee of The Hong Kong Polytechnic University in writing (c/o Research Office of the University) stating clearly the responsible person and department of this study.

Thank you for your interest in participating in this study.

YEUNG Pui Shan, May
Principal Investigator

參與者的選擇和同意

我們邀請 50 至 64 歲懂中文或英文的香港居民參與。如果你是，請繼續調查問卷。
我同意貢獻將版權讓倫敦衛生和熱帶醫學院公共健康政策用作研究。

Participant selection and consent

We are choosing Hong Kong residents aged 50 to 64 who could understand Chinese or English, please continue the questionnaire only if you are. I hereby assign copyright of my contribution for research purposes to the Faculty of Public Health and Policy of the LSHTM.

抽選被訪者 Participant selection

- 請問你係唔係50至64歲的香港人士？（1962年至1949年出生） Ascertain the person is Hong Kong resident aged between 50 to 64 years? (born between 1962 to 1949)
- 解釋研究目的 Explain the research purpose
- 告訴參與是自願的 Tell the person participation is voluntary
- 取得書面或口頭同意 Obtain written or verbal consent

調查不成功原因 Reasons for unsuccessful interview:

- 拒絕 Refuse
- 前兩年未接種疫苗（太多對照個案） Unvaccinated in previous two years (too many controls)
- 溝通困難 Language difficulty
- 聲稱以前完成同樣的調查 Claimed completed the same survey before

請選擇 Please tick box	
1. 我對所附資料的有關步驟已經得到充分的解釋(或理解口頭解釋)。這項研究應不會對我造成任何不適。如果我參加，我明白需要做什麼。我是自願參與這項研究。 I fully understand the information concerning this study (or have understood the verbal explanation). This study should not cause any discomfort. I understand what will be required of me and what will happen to me if I take part in it. My participation is voluntary.	<input type="checkbox"/>
2. 有關於這項研究的問題，已經回答了。 My questions (if any) concerning this study have been answered by the interviewer.	<input type="checkbox"/>
3. 我理解我有權在研究過程中提出問題，并在任何時候決定退出研究而不會受到任何不正常的待遇或被追究責。 I understand I have the right to ask question during the research, and may withdraw from this study without giving a reason and without any unusual treatment or any consequence.	<input type="checkbox"/>
4. 我同意參與由楊貝珊醫生負責監督和執行的研究項目。 I agree to take part in this study supervised and implemented by Dr. YEUNG Pui Shan.	<input type="checkbox"/>

被訪者姓名 Name of participant

訪問員姓名 Name of interviewer

被訪者簽名 Signature of participant

訪問員簽名 Signature of interviewer

日期 Date

日期 Date

以下問題請選擇一個答案，除非另有說明。

Please choose **only one answer** for the following questions unless otherwise stated.

人口統計學 Demographics

1. 你的出生年份係？ What is your year of birth? _____ (1962 to 1949)
2. 請問你性別係？ What is your gender?
(訪問員：喺未能確定被訪者嘅性別嘅情況下才問此問題。)
(Interviewer: Only ask when you are unsure about the participant's gender.)
 - a. 男 Male
 - b. 女 Female
3. 請問你種族？ What is your ethnicity?
 - a. 中國 Chinese
 - b. 印尼 Indonesia
 - c. 菲律賓 Philippines
 - d. 白人 White (American or European)
 - e. 印度人 Indian
 - f. 其他 Other (請說明 Please specify:_____)
4. 請問你最高教育程度？ What is your highest educational attainment?
 - g. 未受教育／幼稚園 No schooling / kindergarten
 - h. 小學 Primary
 - i. 中學 Secondary
 - j. 大專或以上 Tertiary or above
 - k. 拒絕回答 Refuse to answer
5. 請問你現在職業？ What is your current occupation?
(訪問員：如未能分類，填上職業名稱。)
(Interviewer: Write down the name of occupation if you cannot classify.)
 - a. 僱主 / 經理及行政人員 Employer / manager and administrator
 - b. 專業人員 / 輔助專業人員 Professional / Associate professional
 - c. 文員 / Clerk
 - d. 服務工作及商店銷售人員 Service worker and sales
 - e. 技術工人 / 非技術工人 Skilled or unskilled worker
 - f. 學生 Student
 - g. 料理家務者 Homemaker
 - h. 退休人士 Retired
 - i. 待業 Unemployed person
 - j. 其他 Other (請說明 Please specify:_____)
6. 你嘅職業與醫護有關嗎？ Is your occupation health related?
 - a. 有關 Yes
 - b. 冇關 No

7. 你有冇領取綜合社會保障援助（綜援）？
Are you receiving Comprehensive Social Security Assistance (CSSA)?
- 有 Yes
 - 冇 No
8. 請問你每月嘅個人總收入係？ What is your total monthly personal income?
- 沒有收入 No income
 - 港幣\$7,500以下 Below HK\$7,500
 - 港幣 HK\$7,500 – \$9,999
 - 港幣 HK\$10,000 – \$14,999
 - 港幣 HK\$15,000 – \$19,999
 - 港幣 HK\$20,000 – \$29,999
 - 港幣 HK\$30,000以上 or above HK\$30,000
9. 你有冇吸煙？ Are you a smoker?
- 有 Yes
 - 已戒煙 Ex-smoker
 - 從來冇 Never
10. 你有冇飲酒？ Are you a drinker?
- 有社交飲酒 Yes, social drinker
 - 有酗酒 Yes, binge drinking
 - 冇 No
11. 你住哪個區？ Which district do you live?
- | | |
|-----------------------------------|--------------------------------|
| a. 中西區 Central & Western District | j. 深水埗區 Sham Shui Po District |
| b. 東區 Eastern District | k. 南區 Southern District |
| c. 離島區 Islands District | l. 大埔區 Tai Po District |
| d. 九龍城區 Kowloon City District | m. 荃灣區 Tsuen Wan District |
| e. 葵青區 Kwai Tsing District | n. 屯門區 Tuen Mun District |
| f. 觀塘區 Kwun Tong District | o. 灣仔區 Wan Chai District |
| g. 北區 North District | p. 黃大仙區 Wong Tai Sin District |
| h. 西貢區 Sai Kung District | q. 油尖旺區 Yau Tsim Mong District |
| i. 沙田區 Sha Tin District | r. 元朗區 Yuen Long District |

行為 Behaviour

- Q1. 你在過去的兩個疫苗接種季節有冇打流感針（自2011年九月）？
Have you got flu shot in past two vaccination seasons (since 2011 Sep)?
- 有，今年 Yes, this year (2012/13; 即自2012年9月 i.e., since September 2012)
 - 有，這兩年 Yes, for two years (2012/13 and 2011/12, 即自2011年9月 i.e., September 2011)
 - 冇 No

Q2. 你2011/12年以前有沒有打過流感針？ Have you ever received a flu shot before 2011/12?

- a. 有 Yes
- b. 冇 No

Q3. 你會唔會在未來幾個月內打流感針（2013年9月至2014年8月）？

Will you receive flu shot in the coming months (from Sep 2013 to Aug 2014)?

- a. 一定會 Yes, definitely
- b. 可能會 Yes, probably yes
- c. 可能唔會 No, probably not
- d. 一定唔會 No, definitely not

醫療系統 Health-Care System

Q4. 你是否有政府免費或資助打流感針？ Are you eligible for free or subsidized vaccination under the Government Vaccination Programmes and Schemes?

- a. 有 Yes
- b. 冇 No

Q5. 請問你知不知道有政府防疫注射計劃和資助計劃，和非政府的疫苗資助計劃？

Are you awareness of the Government Vaccination Programmes and Schemes; and non-governmental vaccination subsidy schemes?

- a. 有 Yes
- b. 冇 No

Q6. 請問你願意比幾多錢去打流感針呢？

If you need to pay, how much are you willing to pay for receiving a flu shot?

- a. \$0
- b. \$1 - \$50
- c. \$50 - \$100
- d. \$100 - \$150
- e. 費用唔係問題 Cost is not an issue

Q7. 如果打流感針是免費，你願意打嗎？

Are you willing to receiving flu shot if it is FREE?

- a. 願意 Yes
- b. 不願意 No (請說明 Please specify _____)

Q8. 你上次在哪裡打流感針呢？ Where did you got the flu shot last time?

- a. 在政府(公營)診所 In government clinics
- b. 在私人診所 In private clinic
- c. 在醫院 In hospital
- d. 其他地方 (請註明 Please specify: _____)
- e. 沒有打流感針 No, have not receive flu shot

Q9. 到打流感針的地方方便嗎？ Was the access to receive the flu shot convenient?

唔方便 Very inconvenient 好方便 Very convenient
1 2 3 4 5

信念和感覺 Belief and perceptions

Q10. 你認為你喺未來12個月內感染流感嘅機會有幾高呢？

What is your chance of contracting flu in the next 12 months?

很低 Very low 很高 Very high
1 2 3 4 5

Q11. 你預計你流感嘅病情會點樣呢？

What would you expect the severity of the disease to be if you get flu?

- 嚴重 (需要住院/可能會導致死亡) Severe (need hospitalization / may cause death)
- 中等 (需要睇醫生 / 休息 / 影響日常工作) Moderate (need doctor consultation / take rest / affect daily routines)
- 輕微 (輕微病徵，可繼續日常工作) Mild (mild symptoms and can continue daily routines)
- 唔知道 Don't know

Q12. 你認為疫苗是安全和只有輕微的不良反應嗎？

Do you think the vaccine is safe with only minor adverse reaction?

- 是 Yes
- 不是 No

Q13. 你認為流感疫苗有效保護你嗎？

Do you think the vaccine is useful in protect you from flu?

有效 Very useless 有效 Very useful
1 2 3 4 5

Q14. 你覺得打流感針，有其他好處嗎？

Do you think having a flu shot has other benefits?

- 有，保護家人 Yes, protect family
- 有，履行社會規範 Yes, fulfill social norm
- 有，工作需要 Yes, requirement of work
- 有，其他原因 Yes, for other reasons 註明specify: _____
- 有 No

Q15. 你唔打流感針，喺唔喺因為怕打針/怕痛？

Will you not get the vaccine because of scare of needle or pain?

- 怕打針 / 怕痛 Yes
- 唔喺 No

Q16. 你認為你健康嗎？ Do you think your health is good?

唔健康 Very unhealthy 好健康 Very healthy
1 2 3 4 5

需要 Need

Q17. 你有冇任何慢性疾病，如高血壓，糖尿病，高血脂，心臟疾病，殘疾等？
Do you have any chronic illness, e.g., hypertension, diabetes, hyperlipidemia, heart diseases, disability etc?

- a. 有 Yes
- b. 冇 No

Q18. 在過去 3 個月，你需要睇醫生（西醫或中醫）嗎？ Do you need to consult a doctor (Western or Traditional Chinese Practitioner) in the past 3 months?

- a. 只有睇西醫 Yes, only Western doctor
- b. 只有睇中醫 Yes, only Traditional Chinese Practitioner
- c. 有睇兩種醫生 Yes, both types
- d. 冇 No

Q19. 與你家中共同居住，有冇未滿6 歲嘅兒童或者65歲或以上長輩？

Are you living with children <6 years or elders ≥65 years?

- a. 有未滿6 歲嘅兒童 Yes, child / children <6 years
- b. 有未滿65 歲或以上長輩 Yes, elders ≥65 years
- c. 有未滿6 歲嘅兒童和未滿65 歲或以上長輩 Yes, both
- d. 冇 No

知識 Knowledge

Q20. 打流感針能否減少流感並發症及入院？

Can flu shot reduce flu complications and related hospital admission?

- a. 能 Yes
- b. 不能 No

Q21. 請講出有效預防流感嘅方法？你可以選擇多過一個答案。（開放式問題）

Can you list measures that are effective to prevent flu? You can give more than one answer. (open-ended question)

- a. 保持健康生活模式 Maintain healthy lifestyles
- b. 避免人多的地方 Avoid crowd places
- c. 保持室內空氣流通 Maintain good indoor ventilation
- d. 注意個人衛生，例如打噴嚏後洗手 Observe personal hygiene, e.g., wash hand after sneezing and coughing
- e. 服用藥物，例如預防藥物，中藥 Take drugs, e.g., chemoprophylaxis, Chinese herbs
- f. 打流感針 Get a flu shot

- Q22. 你認為你屬唔屬於目標或高危組別嘅人士呢？
Do you think you are the target or high-risk group for flu shot?
- a. 屬於 Yes
 - b. 唔屬於 No

建議和社會支持 **Advice and social support**

- Q23. 如果醫護人員提醒你，你會去打流感針嗎？
Will you go to get a flu shot if health professionals advise you?
- a. 會 Yes
 - b. 唔會 No
- Q24. 如果家人或朋友勸你，你會去打流感針嗎？
Will you go to get a flu shot if your family or friends advise you?
- a. 會 Yes
 - b. 唔會 No
- Q25. 如果有客戶系統提醒你打流感針，你會打針嗎？
Will you get the flu shot if there is a client reminder system to remind you?
- a. 會 Yes
 - b. 唔會 No
- Q26. 與你同居的家庭成員有冇打流感針？
Have your family member in your household received flu shot?
- a. 有 Yes
 - b. 冇 No

外界環境因素 **External environmental factors**

- Q27. 請問您選擇打流感針會受外界因素影響嗎？
Will your choice of receiving flu shot affected by external factors?
- a. 頻繁媒體廣告 Frequent media advertisements
 - b. 近期當地的流行病 Recent local epidemics
 - c. 近期海外流行 Recent overseas epidemics
 - d. 其他 Others (請註明 specify:_____)

*問卷調查結束，謝謝！
End of questionnaire, Thank you!*

Annex 2

Table showing the variables in the case-control study

Predisposing socio-demography		
D1 ^{*****}	Age (years)	Year of birth (continuous) Categories: 18-34, 35-49, 50-64
D2	Sex	Male Female
D3	Ethnicity	Chinese Indonesian Philippines Whit (Am/ Eur) Indian Other (_____)
D4	Highest educational attainment	No schooling / kindergarten Primary Secondary Tertiary or above Refuse
D5	Occupation	Employer / manager & administrator Professional / Associate professional Clerk / administrative office work Service worker and sales Skilled or unskilled worker Student Homemaker Retired Unemployed person Other (_____)
D6	Occupation (Health-related)	Health-care Non-health care
D7	CSSA recipient	Yes, No
D8	Income	No income Below HK\$7,500 HK\$7,500 – \$9,999 HK\$10,000 – \$14,999 HK\$15,000 – \$19,999 HK\$20,000 – \$29,999 HK\$30,000 or above
D11	District	Either 1 of the 18 districts
Knowledge		
4	Know GVP and Scheme	Yes, No
19	Flu reduce hospital admission	Yes, No
20	Flu protection %	0%-19% 20%-49% 50%-69% 70%-89% 90%-100%

***** Indicates question number in the questionnaire.

21	Other measures in preventing flu	Number of total right answers
22	Being recommended group	Yes, No
Need		
16	Presence of chronic diseases	Yes, No
17	Consult a doctor in the past 3 months	Yes, Western Yes, TCM Yes, both No
18	Live with children <6 years or elders ≥65 years	Yes, children Yes, elder Yes, both No
Behaviour		
1	Previous flu vaccination history	Yes, this year (2012/13) Yes, last year (2011/12) Yes, for both years Yes, more than two years ago No
2	Will get flu shot next year	Certainly Maybe Maybe not Certainly not
D9	Smoker	Yes, No
D10	Drinker	Yes, No
Belief & perceptions		
9	Perceived chances of contracting influenza	Scale 1 to 5
10	Perceived severity of influenza	Mild Moderate Severe Don't know
11	Perceived vaccine safety	Yes, No
12	Perceived vaccine adverse events is minor	Yes, No
13	Perceived vaccine effect against flu	Scale 1 to 5
14	Believed flu vaccine has additional benefits other than flu protection	Yes, protect family Yes, work requirement Yes, for other reasons (_____) No
15	Self-assessed health	Scale 1 to 5
Health-care system		
3	Eligibility of using free or subsidised service	Yes, No
5	Willingness of the out-of-pocket vaccine and administration cost	\$0 \$1 - \$50 \$50 - \$100 \$100 - \$150 Cost is not an issue
6	Willing to receive flu shot if it is free	Yes, No

7	Preferred location to have flu shot	Government clinics Private clinic Hospital Other (_____) No
8	Convenience of access to health-care settings	Scale 1 to 5
26	Response to client reminder system	Yes, No
Advice & social support		
23	Advice from health professionals	Yes, No
24	Advice from family and friends	Yes, No
25	Household member receive vaccine	Yes, No
External environment		
27	Any external environmental factors	Frequent media ads Recent local epidemics Recent _____ nearby epidemics Others (specify:_____)

Questions specific for vaccinated and non-vaccinated respondents		
V1a	Reason for vaccination	Health professional advice Unsatisfactory health Belong to high-risk group Vaccine is effective Work requirement Free/ subsidized vaccination Protect family member Other (_____)
V1b	Location to have flu shot last time	Yes, in private clinic Yes, in government clinics Yes, in hospital Yes, elsewhere No
N1c	Reason for non-vaccination	Unnecessary Busy Flu is a mild illness Side effects Vaccine is ineffective Non-high risk group Expensive Do not know where to get it Other (_____)
N1b	Scare about injection	Yes, No

Annex 3

Factors Associated with Uptake of Influenza Vaccine in People Aged 50 to 64 years in Hong Kong: A Case-Control Study

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- Introduction**
 - In Hong Kong, people aged 50 to 64 were added as a recommended priority target group for influenza vaccination by the Department of Health starting from 2011/12. The coverage rate of the influenza vaccine for this age group was 8.5 percent in 2012/13.*
- Objective**
 - To determine which factors were associated with uptake of influenza vaccination amongst adults in Hong Kong aged 50 to 64 years.
- Method**
 - A case-control study was conducted in communities by street intercept interview from 17 July to 15 August 2013. Cases were Hong Kong citizens age 50 to 64 years who received influenza vaccine in 2011/12 or 2012/13. Controls were the same as cases, except they did not receive influenza vaccine in 2011/12 or 2012/13. Multinomial logistic regression analysis was performed to explore the associations (odds ratios) between vaccination status and the variables.

Photos: Locations of the street intercept survey



Infogram of the study result
 The words represent factors (variables) included in this study. The word sizes reflect the magnitudes of the adjusted odds ratio between cases and controls.



- A total of 604 respondents were interviewed and included in the analysis. There were 193 cases (vaccinated) and 411 controls (non-vaccinated), with a case-to-control ratio of 1:2.1. When compared, the factors that were strongly and significantly associated with vaccination are labeled with OR shown in the infogram.
- The majority (89%) of all the respondents were not aware that they belonged to a recommended group for influenza vaccination.
- Eighty percent (80%) of all the respondents were 'willing to receive flu vaccination for free'; and 36.8% were 'willing to pay <HKD\$50 (USD\$6.4) for a flu vaccine'.



- This is a case-control study with vaccination status as the 'outcome' and personal or external environmental factors as 'exposures'. This design is chosen because of the low prevalence of eligible cases (~2%) in the population.
 - The high affordability of an annual influenza vaccine for the general public could be the basis of success on out-of-pocket payment.
 - Better communication of the health risks and need might improve the vaccination rate.
 - Engaging health professionals in vaccine promotion would be an effective measure.
 - Limitation of this study: an overall response rate of 41.7% and the possibility of missing those look "inappropriate" (much younger or older) to age.
- Conclusion**
 Factors related to the existing health-care service, perception on influenza vaccination and advice from health professionals were significantly associated with influenza vaccination uptake amongst 50 to 64 year-olds, compared to other factors.

Table. Compare factors with high odds ratios (OR) in this study and other literatures

Systematic literature review	OR	Case-control study	OR
Presence of chronic disease(s) ^{1,2,3}	1.38-13.7	Eligible for free government vaccine	6.38
Advice from health professionals ^{3,4}	1.23-13.0	Willing to receive flu vaccination for free	4.84
Perceived vaccine efficacy ^{4,5,6}	2.7-10.55	Perceived having severe or moderate symptoms when contracting flu	2.90
Advice from doctors ^{2,4}	4.03-7.82	Convenient to reach a vaccination location	2.87
Free vaccination ^{7,8}	4.5-7.8	Accept advice from health professionals	2.67
Cues to action (relative and friends receive vaccine) ⁴	6.44	Had family member receive flu vaccine	2.47
Perceived chances of contracting influenza ^{6,9}	1.62-5.40	Will receive flu vaccine when there is an epidemic	2.40

Diagram. Policy Implications of this study



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