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An Advisory Committee Statement (ACS)
National Advisory Committee on Immunization (NACI)

APPENDIX 1: EVIDENCE REVIEW ON OCCUPATIONAL EXPOSURE OF SWINE AND POULTRY WORKERS

Please note: The provision of recommendations regarding immunization of swine workers as a means to protect swine herds is not within the scope of NACI. For animal health concerns, the reader should refer to appropriate animal health resources.

Preamble

The National Advisory Committee on Immunization (NACI) provides the Public Health Agency of Canada (hereafter referred to as the Agency) with ongoing and timely medical, scientific and public heath advice relating to immunization. The Agency acknowledges that the advice and recommendations set out in this statement are based upon the best currently available scientific knowledge and is disseminating this document for information purposes. People administering the vaccine should also be aware of the contents of the relevant product monograph(s). NACI recommendations for use and other information set out herein may differ from that set out in the product monograph(s). Manufacturer(s) have sought approval of the vaccine(s) and provided evidence as to its safety and efficacy only when it is used in accordance with the product monographs. NACI members and liaison members conduct themselves within the context of the Public Health Agency of Canada's Policy on Conflict of Interest, including yearly declaration of potential conflict of interest.

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I. Executive Summary

In mid-2012, in response to the emergence of several swine variant influenza strains in humans in the United States of America (USA) (H3N2v, H1N1v, H1N2v) and in Canada (H1N1v) the Public Health Agency of Canada (PHAC) requested the Influenza Working Group (IWG) of the National Advisory Committee on Immunization (NACI) to consider a recommendation for immunization of individuals with occupational exposure to swine and poultry. In Canada, NACI's process for development of influenza immunization recommendations takes into consideration a broad range of available studies and data to make evidence-based recommendations in the evaluation of the safety and efficacy of vaccines for humans. Professional judgment, clinical experience and an overall analysis of risk also influences recommendations. For animal health concerns, the reader should refer to appropriate animal health resources.

To inform this discussion, PHAC and NACI IWG undertook various methods of exploring the question including scientific evidence, best practices, and expert opinion. This report outlines the process, studies, and data used by NACI to develop its recommendation for seasonal vaccination of swine and poultry workers. The evidence includes:

- A rapid review conducted by the Canadian Agency for Drugs and Technologies in Health titled "Influenza Vaccination for Prevention of Cross-species Infection: A Review of the Clinical Evidence"
- A literature review was conducted to identify the prevalence and risk of cross-species transmission of animal influenza A.
- A meeting with animal health experts to understand current vaccination practices of swine and poultry workers, the biosecurity measures used in the industry, and the risk of cross-species influenza transmission.

I.1 OVERVIEW OF MAJOR FINDINGS

- No studies were identified that examined the effectiveness of vaccination of swine and poultry workers on genetic reassortment of influenza virus.
- Transmission of avian or swine influenza from animal populations to occupationally exposed humans occurs, but not frequently.
- Occupationally exposed workers are more likely to be seropositive for avian or swine influenza than unexposed individuals.
- The potential for limited human-to-human transmission exists from infected workers to unexposed household members.
- There is a wide range of seasonal influenza vaccination rates among workers.
- Most Canadian swine veterinarians are members of professional associations that already have position statements in favour of seasonal vaccination, and most veterinarians are aware of these recommendations.
- Canadian farms have strict bio-security measures that are their major means of avian/swine influenza prevention.

I.2 OVERVIEW OF MAJOR LITERATURE REVIEW LIMITATIONS

- Large amount of heterogeneity between studies impacted comparability
- Lack of standard testing protocols for seroresponse to non-human, non-H5N1 strains
  - Studies use different titre cut-offs to identify a positive response
  - Potential for waning immunity and/or cross-protection to impact detection
- Cross-reactivity between swine, avian and human influenza viruses
- Many of the studies were cross-sectional seroprevalence surveys
  - Prevalence of avian or swine influenza viruses in the animal populations or the region was usually not known or its presence was not confirmed
  - Some studies established control groups, but there were comparability issues

I.3 CONCLUSIONS

After discussing the available body of evidence, NACI unanimously decided on the following recommendations:

- *"NACI concludes that there is insufficient evidence at this time to specifically recommend routine influenza immunization for swine workers (NACI recommendation grade I); however NACI encourages influenza vaccine for all Canadians age 6 months and older."*

- *"NACI continues to recommend immunization against seasonal influenza for people in direct contact during culling operations involving poultry infected with avian influenza (NACI recommendation grade I); however NACI encourages influenza vaccine for all Canadians age six months and older".*

These recommendations are reflected in the *Statement on Seasonal Influenza Vaccine for 2013–2014*.

II. Introduction

The genetic reassortment of influenza A viruses from different animal species is thought to be a mechanism for the development of influenza viruses with pandemic potential. Human influenzas and influenza viruses of avian and swine origin mostly circulate exclusively within their respective species. However, influenza viruses possess the ability to infect and potentially transmit themselves in species other than their native host. Influenza A viruses are categorized based on combinations of the two surface proteins hemaglutinin and neuraminidase. In a statistical analysis of 3,874 full-length neuraminidase sequences (N1-N9), Yan et al. (2010)[1] found that there is greater intra-species variation than inter-species variation in some host species. While a number of virus subtypes do not appear to be transmissible between species, some subtypes have a weak barrier, and some have virtually no barrier between species, in nature and in laboratory experiments.

II.1 EPIDEMIOLOGY OF ANIMAL-ORIGIN INFLUENZA VIRUSES

Humans working with live or dead animals that are also reservoirs for influenza, including, but not limited to, poultry and swine, are presumably at higher risk for infecting and being infected by the animals they work with due to their high degree of interaction. The role of animal-origin influenza viruses in causing human illness has been recognized for some time; however, it is unclear how frequently animal influenza viruses are transmitted to humans, or vice versa. The majority of existing surveillance systems are not set up to detect asymptomatic or mild illness in humans caused by human or animal influenzas. As well, swine influenza is not federally reportable in Canada and there is no national human surveillance systems set up to specifically identify swine origin influenza in humans. Despite this, routine testing done in animals and humans does identify emergent influenza strains and some have generated significant interest.

Avian influenza has economic and health implications. Notifiable Avian Influenza (NAI) are identified as all H5 and H7 and any highly pathogenic avian influenza (HPAI) viruses. Low pathogenicity avian influenza (LPAI) viruses are associated with mild or no apparent disease in poultry. HPAI viruses can cause severe illness and high mortality in poultry flocks. Extensive culling measures are usually taken to control NAI viruses (NAIVs), which can be devastating to poultry operations. Currently, the most prolific AIV is highly pathogenic H5N1. Since its emergence in 1997, H5N1 has caused 371 deaths out of 622 confirmed human cases[2] (as of March 12, 2013) and has been heavily monitored as an influenza strain with pandemic potential. To date, however, it has yet to develop the capacity for efficient human-to-human transmission, although it continues to have a high case fatality rate when contracted by humans.

Surveillance of NAIV is fairly well established. The Canadian Notifiable Avian Influenza Surveillance System (CanNAISS) is a joint initiative between government, industry and farmers to prevent, detect, and eliminate H5 and H7 AIV subtypes. CanNAISS meets the notifiable avian influenza guidelines established by the World Organization for Animal Health (OIE) and trade requirements from the European Union.[3]

Unlike AIVs, swine influenza viruses (SwIVs) generally cause few deaths in pigs, but can cause high levels of illness in pig herds. Swine are of particular interest in interspecies transmission of influenza because they possess receptors in the respiratory tract that allow them to contract both human and avian influenza viruses. Transmission of influenza between swine and humans is known to occur, as is transmission from poultry to swine. Swine have historically been considered the ideal mixing vessel for the production of novel viruses; however, recent research reveals that based on receptors alone, swine and humans are equally likely to act as mixing vessels for viral reassortment.[4,5]

In Canada, there are no federal surveillance programs for the detection of influenza in swine, and existing provincial and territorial surveillance programs may vary. A voluntary swine influenza surveillance program was initiated in the US in 2008, operated through the United States Department of Agriculture in collaboration with states and industry. Between October 1, 2010 through July 31, 2012, the program tested 12,662 samples taken from 3,766 swine diagnostic lab submissions (multiple samples from each submission), and found that 1,488 were positive for influenza A infections.[6]

II.2 PANDEMIC RISK

An influenza pandemic is an unpredictable but recurring event that can have a significant impact on the population.[7] It occurs when a novel influenza virus, transmissible to and amongst humans, and against which humans have little to no immunologic protection, spreads widely across the world. Since the 16th century, pandemics have occurred at intervals of 10–50 years.[8] There is no way to predict when a novel influenza strain will emerge and become a pandemic concern, and how severe it may be. The H1N1 influenza strain in the 2009 pandemic was antigenically similar to H1N1 viruses circulating among North America swine, and distinct from seasonal human H1N1 viruses; its genome comprised a reassortment of genes of avian, human and swine origin influenza A viruses.[9] This highlights the role genetic reassortment plays in the evolution of pandemic influenza strains.

II.3 PURPOSE

The objective of this review is to assess the body of evidence around the risk and prevalence of cross-species influenza transmission to and from humans. This review includes a Rapid Response Report from the Canadian Agency for Drugs and Technologies in Health, a literature review on cross-species influenza transmission, and a meeting with members of the Avian Flu Task Group from the joint committee of the Chief Medical Officers of Health, as well as the Chief Veterinary Officers.

III. Methodology

III.1 CADTH RAPID RESPONSE REPORT

In February 2012, PHAC requested that the Canadian Agency for Drugs and Technologies in Health (CADTH) review the clinical evidence regarding the effectiveness of immunization of animal workers to reduce the risk of cross-species influenza infection in humans, and the risk of co-infection with human and animal influenza. There were two research questions:

1. What is the clinical evidence regarding the effectiveness of immunization of animal workers to reduce the risk of cross-species influenza infection in humans?
2. What is the clinical evidence regarding the effectiveness of immunization of animal workers to reduce the risk of co-infection with human and animal influenza?

A limited literature search was conducted using PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination databases, Canadian and major international health technology agencies, as well as a focused Internet search. All study types were considered, and the search was limited to studies published in the English language between January 1, 2007 and January 11, 2012. For a more detailed methodology, please refer to the report.[10]

III.2 LITERATURE REVIEW

Two searches were conducted in each of the following four databases: Medline, Embase, Global Health, and Agricola, for literature published in the English language up until July 3, 2012. The first search focused on swine or avian influenza infection in agricultural or farm workers who work with livestock, and the second search focused on cross-species influenza infection. A total of 273 and 1163 articles were retrieved from the first and second searches respectively. The searches were kept broad to assess the size of the body of evidence that exists on the subject. Following this assessment, additional criteria were applied to narrow the scope of the review. The inclusion criteria for articles of interest were for those that involved cross-species influenza infection to or from humans who raise and/or work with live or dead animals. Articles were excluded if they were not conducting primary research, involved experimental influenza infection, conducted analysis for influenza strains native to the study population (e.g. avian influenza in poultry, human influenza in humans), or were published prior to the year 1997. Please refer to Appendix A for the evidence tables.

A rapid review limited to the English and French language was also conducted to determine which countries currently make an explicit recommendation for animal workers to receive the seasonal influenza vaccination (Appendix B).

III.3 IWG MEETING WITH ANIMAL HEALTH EXPERTS

The Influenza Working Group (IWG) held an ad hoc meeting in December 2012 in order to discuss the current vaccination practices of swine and poultry workers, the biosecurity measures used in the industry, and risk of cross-species influenza transmission with members of the Avian Flu Task Group from the joint committee of the Chief Medical Officers of Health, as well as the Chief Veterinary Officers. Please refer to the discussion for further information.

IV. Results

IV.1 CADTH RAPID RESPONSE REPORT

The literature search yielded a total of 219 citations, 215 of which were excluded after reviewing the titles and citations. Four potentially relevant articles under-went a full text review, as did an article identified in the grey literature. None of these five articles met the inclusion criteria. Some studies examined the effect of influenza vaccines in the general population, healthy volunteers, children, older people, or focused on health care workers, but none focused on animal workers.

IV.2 PHIWG LITERATURE REVIEW

A total of 44 articles meeting the inclusion and exclusion criteria were selected for the review. Thirty-one articles assessed the seroprevalence of AIV in individuals occupationally exposed to poultry flocks or wild birds, and 13 articles assessed SwIV in individuals occupationally exposed to swine. A broad range of individuals with the potential to be occupationally exposed to AIV or SwIV were surveyed including backyard farmers, farmers or workers in commercial farm operations, cullers/slaughterers, meat processors, veterinarians, laboratory analysts, researchers, government workers,[11] firefighters,[11] migratory bird handlers, and bird banders. In both avian and swine exposed individuals, immunological indications of cross-species infection were not detected at high frequencies. Low levels of antibody response in the study population to an animal influenza were detected in a majority of the studies, although some may have been the result of cross-reactivity to exposure to human influenzas. A small number of studies also included an assessment of household members of individuals with confirmed AIV or SwIV as study participants or as control groups.

IV.2.1 Avian influenza virus in individuals occupationally exposed to poultry or wild birds

Of the 31 articles assessing the seroprevalence of AIV in humans, eight assessed seroprevalence of AIV in cullers, slaughterers or individuals collecting dead birds.[11–17] Eighteen articles assessed commercial poultry workers, seven articles assessed non-commercial poultry workers (i.e. backyard farmers), and four studies assessed other workers including bird banders,[18] handlers of migratory birds,[19] firefighters,[11] and government workers[11] involving in culling.

Of the 18 articles involving commercial poultry workers, eight articles considered an individual seropositive if antibody titres were at least ≥1:10. Another eight articles characterized seropositivity with titers at least ≥1:80. One article had undisclosed seropositivity conditions, and another article collected information on symptoms only. Noting the difference in use of titre thresholds is important as at present, a titre of ≥1:80 is the recommended threshold for assessing potential H5N1 infection. No other recommendations exist for other avian influenza strains, although some articles used the H5N1 recommendations as a guideline for their laboratory tests. A few of the other studies used a threshold of ≥1:80, but these were grouped with the 1:80 studies for comparative purposes.

Overall, the seroprevalence of AIV was typically low (<1% of participants), but some serological activity was detected in a majority of the studies. Two articles using an antibody titre threshold ≤1:80 did not find any evidence of serological activity. Four articles using a threshold of ≥1:80 reported having participants with low levels of serological activity, but none met the conditions for seropositivity.

In the small number of studies assessing both poultry workers and cullers, cullers constituted the majority of seropositive cases. Alizadeh et al (2009) found seropositivity for AIV in slaughter-house workers to be 2.09 times higher than in poultry workers (51.6% vs. 24.6%) among the 48/127 workers who tested positive for H9N2 (titres ≥1:20).12 During an outbreak of H5N1 in South Korea, the 9/2512 positive cases (titres ≥1:80) were all cullers.15 In a study by Schultsz et al (2009), 3/317 cullers involved in culling for more than one year presented with microneutralization (MN) titres of 1:20, 1:40 and 1:200. None of the 183 poultry workers showed positive titre against H5N1.17 However, a study in rural Cambodia, done by Vong et al (2006), identified slaughtering chickens as a non-significant risk factor for seropositivity after controlling for exposures such as cleaning up cages/stalls, handling live poultry, purchasing live poultry, and cleaning up poultry feathers.[20]

Among studies looking at non-commercial poultry workers (i.e. backyard farmers), four of the seven studies found low levels of serological activity to AIV, but the remaining three did not.

The four studies investigating AIV in other workers (i.e. non-farming) demonstrated serological activity against AIV in a small number of their participants.

IV.2.2 Secondary transmission of AIV

Four of the 30 avian studies tested household contacts of workers for potential AIV infection. Among 28 family members of five confirmed H5N1 cases, only one individual produced a positive sample by MN assay.[21] In another study, 56 out of 62 household members (who had no exposure to poultry) of poultry workers with confirmed A/H7N7 submitted a serum sample at least three weeks after diagnosis of the primary case. Of the 62 individuals, eight reported health complaints and two met the case definitions for both conjunctivitis and ILI. Of the 56 individuals who provided a serum sample, 33 had detectable antibodies against H7.[22] A sample of workers taken from an existing Agricultural Health Survey being conducted in Iowa used the unexposed spouses of the rural agriculture workers exposed to poultry as their comparison group. Over a 24 month period, three individuals in the control group demonstrated titre levels ≥1:20 for H4, H5, H6, and H9. One individual had a titre of ≥1:80 to H9.[23] Outbreak surveillance during an H7 outbreak in the Netherlands in 2003 confirmed A/H7 in three household contacts of a poultry worker or farmer.[24]

IV.2.3 Swine influenza virus in individuals occupationally exposed to swine

Thirteen of the 43 articles assessed the seroprevalence of SwIV in humans. Eleven studies were conducted in workers from commercial farms, and two studies were conducted in community farms. Seropositive individuals were detected in all studies, and Gray et al (2007) was able to isolate SwIV from a symptomatic individual.[25] The number of individuals found to be seropositive to at least one SwIV ranged between 1–2 individuals to up to 47 individuals, depending on the study.

Beaudoin et al (2010) compared employees from two large, comparable swine farms, where one farm was known to have H2N3-positive swine. Four participants were H2N3 positive, only one of which worked on the exposed farm. It was postulated that seropositivity may have been unrelated to recent exposure. Three of the four participants were born before 1968, with the individual who worked on the exposed farm born in 1949; serological activity could be the result of cross-reactivity to previously circulating human H2N3.

Although individuals with swine exposure did produce a greater serological response, Gerloff et al (2011)[26] did not detect a statistically significant difference between the serological responses of healthy individuals with past or present professional exposure to swine and control serum samples from the general population.

IV.2.4 Secondary transmission of SwIV

Two articles evaluated potential household transmission of SwIV from workers. Using a sample of swine workers and their unexposed spouses from the Iowa Agriculture Health Survey, spouses were at an increased risk for H1N1 SwIV compared to unexposed university controls, with adjusted odds ratio of 28.2 (95% CI: 6.1, 130.1). Swine workers had an adjusted odds ratio of 54.9 (95% CI: 12.0, 232.6).[25] Robinson et al (2007)[27] investigated members of a communal farm where an infant had been hospitalized due to a swine-related influenza virus (confirmed). Eight members from three households (including four members from the household of the index patient) were seropositive (titres ≥32). Most had no exposure to swine or <1 hour per week of exposure. One of ten swine serum samples tested was seropositive for the same strain that infected the index patient.[27]

IV.2.5 Influenza vaccination among all occupationally exposed individuals

Information on vaccination history was collected in 22 of the studies and results ranged from workers receiving seasonal influenza in the past year, to never having received seasonal influenza vaccine. One study asked specifically about receiving the 1976 swine influenza vaccine. Vaccination rates ranged from 0 to approximately 60% in the study population. In control groups, vaccination rates were as high as 76%.[18] The wide variation in vaccination rates can potentially be attributed to factors such as vaccine access, living in an urban or rural region, keeping a backyard farm or working on a commercial farm.

IV.2.6 Existing influenza vaccination recommendations for occupationally exposed individuals

From a rapid review limited to the English and French language, a small number of countries have existing national recommendations for seasonal influenza vaccination that specifically mention workers with occupational exposure to animals (Appendix B).

In Canada, NACI recommends that people in direct contact with infected poultry during culling operations, such as cullers, supervising veterinarians and inspectors, receive influenza vaccination. The Canadian Food Inspection Agency (CFIA) uses the broader NACI statement that encourages all healthy Canadians aged 6 months and older get the seasonal vaccine, to encourage all individuals involved in the food production system (e.g. producers and their families, farm workers, veterinarians, farm service personnel, people visiting swine operations) to receive the vaccine as a biosecurity measure.

In the United States, the Centers for Disease Control and Prevention (CDC) issued a statement in 2010 that made a universal recommendation for seasonal influenza vaccination which also explicitly recommended that persons who are charged with responding to avian influenza outbreaks in poultry receive the seasonal influenza vaccine.[28] The 2012 update to the statement did not address this recommendation.[29] With the recent activity involving the 2011 H3N2 variant virus, the CDC released interim guidance for workers employed at commercial swine farms recommending seasonal influenza vaccination for the purposes of reducing the risk of transmitting seasonal influenza viruses from ill people to pigs.[30]

In Australia, the Australian Immunisation Handbook recommends seasonal influenza vaccination during confirmed avian influenza activity to individuals involved in the commercial poultry industry or in culling. However, this recommendation is not stated in the annual seasonal influenza statements produced by the Australian Technical Advisory Group on Immunisation (ATAGI).

The Hong Kong Department of Health recommends seasonal influenza vaccine for poultry farmers and additionally to pig farmers and individuals in the pig-slaughtering industry.

Beginning in the 2006/07 season, an annual seasonal influenza program was implemented in the United Kingdom for poultry workers. However, because of difficulties running the program and low vaccine uptake, the program ended after the 2010/11 season. The recommendation for vaccinating poultry workers, considered a low priority group, was also rescinded. Swine workers were assessed in 2006 and 2009 as a potential target group for vaccination, but no recommendation has been made by the Joint Committee on Vaccination and Immunisation due to limited evidence.

The number of countries sampled was limited by the language restrictions placed on the search. An analysis was conducted by the Vaccine European New Integrated Collaboration Effort Project of national influenza vaccination polices across the European Union, Norway and Iceland in 2009.[31] Of the 27 countries surveyed, 13 (48%) recommended seasonal influenza vaccine for workers in the poultry industry, and 9 (33%) recommended vaccination for individuals in veterinary services. In a second survey, to which 26 countries responded, 4 countries (15%) recommend that families raising poultry also receive the influenza vaccine. However, recommendations are often in flux and the authors noted that several countries had modified their vaccination policies since the initial surveys were conducted.

IV.3 IWG MEETING WITH ANIMAL HEALTH EXPERTS

The IWG held an ad hoc meeting in December 2012 in order to discuss the current vaccination practices of swine and poultry workers, the biosecurity measures used in the industry, and risk of cross-species influenza transmission with members of the Avian Flu Task Group from the joint committee of the Chief Medical Officers of Health, as well as the Chief Veterinary Officers. The following is a synopsis of that discussion.[32,33]

Most Canadian swine veterinarians are members of professional associations that already have position statements in favour of seasonal vaccination, and most veterinarians are aware of these recommendations. The uptake is unknown, however. The Canadian Swine Health Board issued a press release encouraging all barn staff and veterinarians to be vaccinated. They held a vaccination clinic at their October 2012 meeting, and some Canadian swine workers are aware of the board's encouragement to have their influenza vaccination.

Many larger farms in the swine industry already require their staff to be vaccinated against influenza, but it is difficult to mandate and so, in general, they make recommendations, offer vaccination clinics and try to educate staff. After H1N1, it has become more widely accepted that humans may be a source of influenza infection for swine. Some swine farms now will not allow people to enter the barns if they have symptoms of influenza like illness.

The way humans and pigs interact in Canada is slightly different than the way they interact in the USA. Canada has a smaller pig industry, a smaller human population, and fewer farm fairs. As a result, there are fewer human-swine interactions involving the general public. Canadian farms generally have stricter biosecurity measures and most swine are confined to the indoors all year due to the colder weather. Many areas vaccinate their swine, although not always on an annual basis due to cost. Swine influenza strains do not tend to change rapidly from year to year in many regions of Canada. However in areas where high numbers of pigs are produced in large farming systems, influenza strains change rapidly, often requiring autogenous vaccination to control symptoms. This is a more common scenario in the USA with its much larger pig production industry. Swine vaccines have the same efficacy challenges as those made for humans; they do not induce protection against other influenza virus strains that can affect the herd. In regions where farms are more spread out, there is less swine influenza virus transmission than in regions where farms are located closer together. There are much regional variation in the distance between farms across both the USA and Canada.

Bio-security is the major means of prevention of avian influenzas as well. Notifiable avian influenza is reportable in Canada and there is surveillance and the authority to respond if an outbreak is detected, regardless of the pathogenicity. Some producers have their own recommendation that a worker be vaccinated before starting to work with poultry, but these recommendations are not mandatory. In contrast to swine, influenza viruses are not routinely found in commercial poultry in Canada. Birds are not as susceptible to infection with human influenza viruses due to differences between avian and mammalian receptors. Mammals (e.g. swine, ferrets, dogs, cats) are more likely to share influenza viruses with humans.

There is also a growing segment of the human population in both Canada and the USA that is raising pigs and poultry on a smaller scale outside of the commercial industry. These are often referred to as "backyard producers" and usually sell their products at local farmer's markets or directly to the public. They frequently advertise their products as being healthier than products from the commercial industry, and thus do not always see a need for biosecurity or disease control. These producers may not be as well informed about biosecurity or disease, and often apply fewer biosecurity measures. The general public often can directly contact the live animals on these farms. Because this segment is not represented by an industry organization, they can be more difficult to reach and educate.

V. Discussion

The Rapid Response Report conducted by CADTH was based upon a limited literature search and was not a comprehensive, systematic review. It did provide a summary of the current lack of evidence on the topic of influenza vaccination of animal workers for prevention of cross-species infection. As there is no evidence, no conclusions can be drawn regarding the effectiveness of vaccinating this group of workers.

The transmission of avian and swine influenza to the humans that handle these animals is documented in the literature, but because of a number of study limitations, the true extent of the burden of cross-species transmission is difficult to determine.

One limitation of the literature review is due to the fact that standard testing protocols for assessing human immune response to influenza strains that have not adapted to human-to-human transmission do not exist, with the exception of H5N1.[34] This is a significant issue impacting study comparability as authors take different approaches to assess immunological outcomes. Some authors assume that an individual infected with an animal influenza strain would generate low antibody titres that return to pre-infection levels within a short period of time. In these cases, lower cut-offs were used to determine seropositivity (e.g. titres ≥1:10 or ≥1:20). Other studies used existing testing protocols as a guideline, and used higher cut-offs (e.g. titres ≥1:80 or ≥1:160), which could potentially underestimate the frequency of cross-species infection.

The type of assay used to titre antibody responses also affects results. MN assays were considered by some studies to be the preferred assay for assessing seroresponse because it is highly sensitive and specific. Almost all studies used the hemaglutination inhibition (HI) assay,[35] but varied the erythrocyte species used. The HI assay is strain dependent, and if there is a mismatch between the assay and sample strains, the assay is limited in its ability to detect an immune response in an individual who was otherwise infected and capable of mounting a response.

Cross-reactivity between swine, avian and human influenza viruses is another confounding factor that only one study accounted for, which may lead to an erroneous increase in positive results. It can be difficult to identify the potential cross-reactions that could occur, thereby limiting the ability to tease out the impact it may have on the outcome. Cross-reactivity may be more significant in SwIV-related studies. Although there were a limited number of studies, seroresponse to SwIV appeared to be more prevalent than seroresponse to AIV. One study noted that age may be a factor as older individuals may have acquired immunity to influenza strains of interest that possibly re-emerged after a dormant period,[36] and another alluded to the role of influenza vaccination causing cross-reactions during testing.

The discussion with the members of the Avian Flu Task Group and the Chief Veterinary Officers indicated that there are current seasonal vaccination recommendations in place by the various professional associations, and that most veterinarians are aware of these recommendations. The uptake, however, is unknown. The strict biosecurity measures in Canada are the major means of prevention of avian and swine influenza infection.

VI. Recommendations/Rationale

Direct contact with infected poultry, or surfaces and objects contaminated by their droppings, is currently considered the primary route through which workers become infected with avian influenza. As cullers are in an environment with a high concentration of infected poultry, surfaces and objects, this presents an opportunistic setting for viral transmission. Infected poultry can shed large quantities of virus in their droppings and respiratory secretions, and the culling process may result in a higher than normal exposure to these secretions. Influenza is endemic to the swine population and infections are often mild or asymptomatic. Swine and poultry workers are not likely to experience the same intensity of exposure to virus particles as are cullers. It was noted in the literature review that poultry cullers had more frequent positive serology results against avian influenza than other poultry workers. For these reasons, the recommendations for poultry works involved in culling operations differ from those made for poultry and swine workers.

VI.1 POULTRY WORKERS

NACI continues to recommend immunization against seasonal influenza for people in direct contact during culling operations involving poultry infected with avian influenza (NACI recommendation grade I); however NACI encourages influenza vaccine for all Canadians age 6 months and older.

Based on a review of the literature and a discussion with animal health experts, NACI has concluded that there is no direct evidence of the efficacy of vaccinating poultry workers to prevent reassortment of avian and seasonal human strains in humans leading to emergence of pandemic viruses. However, the literature documents the transmission of avian influenza to humans that manipulate poultry as a food source. The contact is usually close and sustained with the animal (for example, culling); and the risk of transmission is relatively low. In the small number of studies that assessed both poultry workers and cullers, cullers constituted the majority of the seropositive cases. It can be hypothesized that contact between a worker involved in culling poultry that are infected with avian influenza would be more prolonged and significant than other types of contact with poultry.

There is evidence that avian and human viruses can reassort and that this reassortment can occur in humans. Influenza does not usually circulate in commercial poultry in Canada and all highly pathogenic avian and any avian strain of H5, H7 are reportable in Canada according to the animal health experts that NACI consulted. Many jurisdictions internationally have a similar recommendation. Based on what is currently known about influenza viruses and reassortment, NACI is of the opinion that immunizing poultry workers against seasonal influenza could prevent reassortment in humans between the avian strain in an outbreak and seasonal strains in humans. However, given the variable efficacy of the seasonal influenza vaccine in healthy adults and in adults with chronic health conditions, the two week period from immunization to development of immunity and the theoretical benefit, seasonal influenza immunization to prevent reassortment of viral strains should be used as a complementary measure to other biosecurity measures that have been described elsewhere (e.g. antivirals and personal protective equipment).[37] Also, seasonal influenza vaccine should not be expected to be efficacious against avian strains of influenza given the significant antigenic difference between strains (e.g. H7N3, H9N2).

VI.2 SWINE WORKERS

NACI concludes that there is insufficient evidence at this time to specifically recommend routine influenza immunization for swine workers (NACI recommendation grade I); however NACI encourages influenza vaccine for all Canadians age 6 months and older.

Based on a review of the literature and a discussion with animal health experts, NACI has concluded that there is currently no direct evidence that immunizing these workers would prevent the emergence of pandemic strains. This would also not be feasible to study. However, based on what is known about transmission and reassortment of swine and human strains, from a theoretical perspective there could be a benefit.

Notwithstanding this statement, NACI continues to encourage influenza vaccine for all Canadians six months of age and older to provide protection to those who wish to take advantage of this vaccine.

The provision of recommendations regarding immunization of swine workers as a means to protect swine herds is not within the scope of NACI. For animal health concerns, the reader should refer to appropriate animal health resources.

Objectives of immunization of swine workers against seasonal influenza can vary:

- Protecting the herds against human strains of influenza;
- Protecting the workers against antigenically related emerging swine strains; and/or
- Preventing reassortment of swine and human strains into pandemic strains.

The burden of transmission between swine and workers in Canada is not well known. Unlike influenza outbreaks in poultry, swine outbreaks of influenza are not reportable in Canada. One study carried out in Alberta in a limited number of commercial farms concluded that the transmission risk from swine to workers and vice versa was low.[38] According to the animal experts with whom NACI consulted, farming operations in Canada involving swine usually apply several biosecurity measures. However, the protection attributable to the human vaccine compared to the other biosecurity measures is unknown. Also, compared to other jurisdictions, the opportunity for direct contact between live swine and the general public is limited in Canada. However, not all farms will apply biosecurity measures equally and there will be some unprotected workers exposed directly to swine in close quarters on a daily basis in Canada. Transmission of swine virus variants to swine workers and their close contacts has been documented in the literature. Because many influenza infections in humans and swine are likely not reported or confirmed, transmission may be underreported in the literature. In conclusion, the risk of influenza transmission between people and swine is likely low for the general public in Canada. Swine workers in both commercial and backyard operations will be at a higher risk than the general public.

Few countries have implemented a recommendation for the seasonal vaccination of swine workers. During the 2006/2007 influenza season, the United Kingdom implemented an annual seasonal influenza program for poultry workers, but the program ended after the 2010/2011 season due to logistical issues, low vaccine uptake, and the consideration that poultry workers are seen as a low priority group. In Canada, recommendations vary: some provinces currently recommend immunization of swine workers; one province recommends against immunization, and one province had a recommendation and then removed it following studies in 2009 that showed an association between receipt of seasonal immunization and infection with pandemic H1N1 strain.[39] Some studies have shown similar results in ferrets and swine after receiving a seasonal vaccine and being challenged with the pandemic H1N1 2009 strain.[40,41] CFIA recommends immunization of swine workers against seasonal influenza. One reason for this is to protect the herds against infection with human influenza strains. However, this is outside of the scope of NACI.

In the context of the emergence of a swine variant virus, the effectiveness of influenza immunization of swine workers would largely depend on the antigenic similarity between the emergent strain and the seasonal influenza vaccine formulation available that particular season.

NACI concludes that with the emergence of a swine variant virus, the virulence of the disease for both swine and humans and vaccine effectiveness in humans are likely to vary and would need to be assessed on a case by case basis to determine if the risk benefit profile favors an immunization recommendation.

Finally, the safety of the influenza vaccine has been documented in adults and important adverse events are quite uncommon, the most common side effect being minor pain at the site of injection for a few days following intra muscular injection. The safety section of the 2013–2014 Influenza Statement can be consulted for more details about the safety of these vaccines.

References

(1) Yan S, Wu G. Evidence obtained from ANOVA to reason cross-species infection and cross-subtype mutation in neuraminidases of influenza A viruses. *Transbound Emerg Dis*. 2010;57(4):254–261.

(2) World Health Organization. Cumulative number of confirmed human cases of avian influenza A(H5N1) reported to WHO, 2013 www.who.int/influenza/human_animal_interface/H5N1_cumulative_table_archives/en.

(3) Canadian Food Inspection Agency. Avian Influenza Surveillance www.inspection.gc.ca/animals/terrestrial-animals/diseases/surveillance/avian-influenza-surveillance/eng/1329693810008/1329694298513, 2013.

(4) Nelli RK, Kuchipudi SV, White GA, Perez BB, Dunham SP, Chang KC. Comparative distribution of human and avian type sialic acid influenza receptors in the pig. *BMC Vet Res*. 2010;6:4-6148-6-4.

(5) Van Poucke SG, Nicholls JM, Nauwynck HJ, Van Reeth K. Replication of avian, human and swine influenza viruses in porcine respiratory explants and association with sialic acid distribution. *Virol J*. 2010;7:38-422X-7-38.

(6) United States Department of Agriculture: Animal and Plant Health Inspection Service. Swine Influenza Surveillance www.aphis.usda.gov/animal_health/animal_dis_spec/swine/siv_surveillance.shtml 2013.

(7) World Health Organization. Pandemic influenza preparedness and response: WHO guidance document. 2009.

(8) World Health Organization. Avian influenza: Assessing the pandemic threat. 2005.

(9) Garten RJ, Davis CT, Russell CA, et al. Antigenic and genetic characteristics of swine-origin 2009 A(H1N1) influenza viruses circulating in humans. *Science*. 2009;325(5937):197–201.

(10) Canadian Agency for Drugs and Technologies in Health (CADTH). Influenza vaccination for prevention of cross-species infection: A review of the clinical evidence. 2012.

(11) Cai W, Schweiger B, Buchholz U, et al. Protective measures and H5N1-seroprevalence among personnel tasked with bird collection during an outbreak of avian influenza A/H5N1 in wild birds, Ruegen, Germany, 2006. *BMC Infectious Diseases*. 2009;9:170.

(12) Alizadeh E, Kheiri MT, Bashar R, Tabatabaeian M, Hosseini SM. Avian influenza (H9N2) among poultry workers in Ian. *Iranian Journal of Microbiology; 2009.1: 3, 3–6.13 ref*. 2009.

(13) Arzey GG, Kirkland PD, Arzey KE, et al. Influenza virus a (H10N7) in chickens and poultry abattoir workers, Australia. *Emerging Infectious Diseases*. 2012;18(5):814–816.

(14) Bridges CB, Lim W, Hu-Primmer J, et al. Risk of influenza A (H5N1) infection among poultry workers, Hong Kong, 1997–1998. *J Infect Dis*. 2002;185(8):1005–1010.

(15) Kwon D, Lee J-, Choi W, et al. Avian influenza A (H5N1) virus antibodies in poultry cullers, South Korea, 2003–2004. *Emerging Infectious Diseases*. 2012;18(6):986–988.

(16) Ortiz JR, Katz MA, Mahmoud MN, et al. Lack of evidence of avian-to-human transmission of avian influenza A (H5N1) virus among poultry workers, Kano, Nigeria, 2006. *J Infect Dis*. 2007;196(11):1685–1691.

(17) Schultsz C, Nguyen VD, Hai le T, et al. Prevalence of antibodies against avian influenza A (H5N1) virus among cullers and poultry workers in Ho Chi Minh City, 2005. *PLoS ONE*. 2009;4(11):e7948.

(18) Gray GC, Ferguson DD, Lowther PE, Heil GL, Friary JA. A national study of US bird banders for evidence of avian influenza virus infections. *Journal of Clinical Virology*. 2011;51(2):132–135.

(19) Shafir SC, Fuller T, Smith TB, Rimoin AW. A national study of individuals who handle migratory birds for evidence of avian and swine-origin influenza virus infections. *J Clin Virol*. 2012;54(4):364–367.

(20) Vong S, Coghlan B, Mardy S, et al. Low frequency of poultry-to-human H5NI virus transmission, Southern Cambodia, 2005. *Emerging Infectious Diseases*. 2006;12(10):1542–1547.

(21) Ceyhan M, Yildirim I, Ferraris O, et al. Serosurveillance study on transmission of H5N1 virus during a 2006 avian influenza epidemic. *Epidemiology & Infection*. 2010;138(9):1274–1280.

(22) Du Ry van Beest Holle,M., Meijer A, Koopmans M, de Jager CM. Human-to-human transmission of avian influenza A/H7N7, the Netherlands, 2003. *Euro surveillance : bulletin europeen sur les maladies transmissibles = European communicable disease bulletin*. 2005;10(12):264–268.

(23) Gray GC, McCarthy T, Capuano AW, Setterquist SF, Alavanja MC, Lynch CF. Evidence for avian influenza A infections among iowa's agricultural workers. *Influenza and other Respiratory Viruses*. 2008;2(2):61–69.

(24) Koopmans M, Wilbrink B, Conyn M, et al. Transmission of H7N7 avian influenza A virus to human beings during a large outbreak in commercial poultry farms in the Netherlands. *Lancet*. 2004;363(9409):587–593.

(25) Gray GC, Trampel DW, Roth JA. Pandemic influenza planning: Shouldn't swine and poultry workers be included? *Vaccine*. 2007;25(22):4376–4381.

(26) Gerloff NA, Kremer JR, Charpentier E, et al. Swine influenza virus antibodies in humans, Western Europe, 2009. *Emerging Infectious Diseases*. 2011;17(3):403–411.

(27) Robinson JL, Lee BE, Patel J, et al. Swine influenza (H3N2) infection in a child and possible community transmission, Canada. *Emerging Infectious Diseases*. 2007;13(12):1865–1870.

(28) Centers for Disease Control and Prevention (CDC). Morbidity and mortality weekly report—prevention and control of influenza with vaccines: Recommendations of the advisory committee on immunization practices (ACIP), 2010. August 6, 2010/59(rr08);1–62.

(29) Centers for Disease Control and Prevention (CDC). Morbidity and mortality weekly report—prevention and control of influenza with vaccines: Recommendations of the advisory committee on immunization practices (ACIP)—United States, 2012–13 influenza season. 2012;61(32);613–618.

(30) Centers for Disease Control and Prevention (CDC). CDC interim guidance for workers who are employed at commercial swine farms: Preventing the spread of influenza A viruses, 2011.

(31) Mereckiene J, Cotter S, D'Ancona F, et al. Differences in national influenza vaccination policies across the European Union, Norway and Iceland 2008–2009. *Eurosurveillance*. 2010;15(44).

(32) NACI Influenza Working Group. Record of decisions December 17th, 2012.

(33) NACI Influenza Working Group. Anonymous .

(34) Global Influenza P. Expert consultation on diagnosis of H5N1 avian influenza infections in humans. *Influenza & Other Respiratory Viruses*. 2007;1(4):131–138.

(35) Rowe T, Abernathy RA, Hu-Primmer J, et al. Detection of antibody to avian influenza A (H5N1) virus in human serum by using a combination of serologic assays. *J Clin Microbiol*. 1999;37(4):937–943.

(36) Beaudoin A, Gramer M, Gray GC, Capuano A, Setterquist S, Bender J. Serologic survey of swine workers for exposure to H2N3 swine influenza A. *Influenza and other Respiratory Viruses*. 2010;4(3):163–170.

(37) Canadian Food Inspection Agency. Animal Biosecurity www.inspection.gc.ca/animals/terrestrial-animals/biosecurity/eng/1299868055616/1320534707863, 2013–02–05.

(38) J. Keenliside. NACI IWG. Communication regarding unpublished Canadian swine influenza study, April 29, 2013.

(39) Skowronski DM, de Serres G, Crowcroft NS, et al. Association between the 2008–09 seasonal influenza vaccine and pandemic H1N1 illness during spring-summer 2009: Four observational studies from Canada. *PLoS Medicine*. 2010;7(4).

(40) Ellebedy AH, Ducatez MF, Duan S, et al. Impact of prior seasonal influenza vaccination and infection on pandemic A (H1N1) influenza virus replication in ferrets. *Vaccine*. 2011;29(17):3335–3339.

(41) Zhu H, Wang J, Zheng Z, et al. Pathogenicity and transmissibility of the pandemic H1N1 2009-related influenza viruses in mice, ferrets, and pigs. *Influenza & Other Respiratory Viruses*. 2011;5(Suppl 1):82–84.

(42) Dejpichai R, Laosiritaworn Y, Phuthavathana P, et al. Seroprevalence of antibodies to avian influenza virus A (H5N1) among residents of villages with human cases, Thailand, 2005. *Emerging Infectious Diseases*. 2009;15(5):756–760.

(43) Gray GC, McCarthy T, Capuano AW, Setterquist SF, Alavanja MC, Lynch CF. Evidence for avian influenza A infections among Iowa's agricultural workers. *Influenza & Other Respiratory Viruses*. 2008;2(2):61–69.

(44) Hinjoy S, Puthavathana P, Laosiritaworn Y, et al. Low frequency of infection with avian influenza virus (H5N1) among poultry farmers, Thailand, 2004. *Emerg Infect Dis*. 2008;14(3):499–501.

(45) Holle, M. R. D. R. van B., Setiawaty V, Pangesti KNA, Sedyaningsih ER. Seroprevalence of avian influenza A/H5N1 among poultry farmers in rural Indonesia, 2007. *Southeast Asian Journal of Tropical Medicine and Public Health; 2010.41: 5, 1095–1103.14 ref*. 2010.

(46) Huo X, Zu R, Qi X, et al. Seroprevalence of avian influenza A (H5N1) virus among poultry workers in Jiangsu province, China: An observational study. *BMC Infectious Diseases*. 2012;12.

(47) Jia N, de Vlas SJ, Liu YX, et al. Serological reports of human infections of H7 and H9 avian influenza viruses in Northern China. *Journal of Clinical Virology*. 2009;44(3):225–229.

(48) Kayali G, Ortiz EJ, Chorazy ML, Gray GC. Evidence of previous avian influenza infection among US turkey workers. *Zoonoses and public health*. 2010;57(4):265–272.

(49) Kayali. Evidence of infection with H4 and H11 avian influenza viruses among Lebanese chicken growers. *PLoS ONE*. 2011;6(10):e26818.

(50) Khuntirat BP, Yoon InKyu, Blair PJ, et al. Evidence for subclinical avian influenza virus infections among rural Thai villagers. *Clinical Infectious Diseases*. 2011.

(51) Koopmans M, Wilbrink B, Conyn M, et al. Transmission of H7N7 avian influenza A virus to human beings during a large outbreak in commercial poultry farms in the Netherlands. *Lancet*. 2004;363(9409):587–593.

(52) Leibler JH, Silbergeld EK, Pekosz A, Gray GC. No evidence of infection with avian influenza viruses among US poultry workers in the Delmarva Peninsula, Maryland and Virginia, USA. *J Agromed*. 2011;16(1):52–57.

(53) Lu CiYong, Lu JiaHai, Chen WeiQing, et al. Potential infections of H5N1 and H9N2 avian influenza do exist in Guangdong populations of China. *Chin Med J*. 2008(Beijing):121: 20, 2050–2053. 18 ref.

(54) Ogata T, Yamazaki Y, Okabe N, et al. Human H5N2 avian influenza infection in Japan and the factors associated with high H5N2-neutralizing antibody titer. *Journal of Epidemiology; 2008.18: 4, 160–166.20 ref*. 2008.

(55) Ortiz EJ, Kochel TJ, Capuano AW, Setterquist SF, Gray GC. Avian influenza and poultry workers, Peru, 2006. *Influenza and other respiratory viruses*. 2007;1(2):65–69.

(56) Ortiz JR, Katz MA, Mahmoud MN, et al. Lack of evidence of avian-to-human transmission of avian influenza A (H5N1) virus among poultry workers, Kano, Nigeria, 2006. *J Infect Dis*. 2007;196(11):1685–1691.

(57) Pawar SD, Tandale BV, Raut CG, et al. Avian influenza H9N2 seroprevalence among poultry workers in Pune, India, 2010. *PLoS ONE*. 2012;7 (5), 18 May 2012.

(58) Puzelli S, Di Trani L, Fabiani C, et al. Serological analysis of serum samples from humans exposed to avian H7 influenza viruses in italy between 1999 and 2003. *J Infect Dis*. 2005;192(8):1318–1322.

(59) Santhia K, Ramy A, Jayaningsih P, et al. Avian influenza A H5N1 infections in Bali province, Indonesia: A behavioral, virological and seroepidemiological study. *Influenza and other respiratory viruses*. 2009;3(3):81–89.

(60) Wang M, Fu CX, Zheng BJ. Antibodies against H5 and H9 avian influenza among poultry workers in China. *N Engl J Med*. 2009;360(24):2583–2584.

(61) Yamazaki Y, Doy M, Okabe N, et al. Serological survey of avian H5N2-subtype influenza virus infections in human populations. *Arch Virol*. 2009;154(3):421–427.

(62) Ayora-Talavera G, Cadavieco-Burgos JM, Canul-Armas AB. Serologic evidence of human and swine influenza in Mayan persons. *Emerging Infectious Diseases*. 2005;11(1):158–161.

(63) Gray GC, McCarthy T, Capuano AW, et al. Swine workers and swine influenza virus infections. *Emerging Infectious Diseases*. 2007;13(12):1871–1878.

(64) Kitikoon P, Sreta D, Tuanudom R, et al. Serological evidence of pig-to-human influenza virus transmission on Thai swine farms. *Vet Microbiol*. 2011;148(2–4) (pp 413–418):ate of Pubaton: 24 Mar 2011.

(65) Krumbholz A, Lange J, Durrwald R, et al. Prevalence of antibodies to swine influenza viruses in humans with occupational exposure to pigs, Thuringia, Germany, 2008–2009. *J Med Virol*. 2010;82(9):1617–1625.

(66) Lopez-Robles G, Montalvo-Corral M, Caire-Juvera G, Ayora-Talavera G, Hernandez J. Seroprevalence and risk factors for swine influenza zoonotic transmission in swine workers from northwestern Mexico. *Transbound Emerg Dis*. 2012;59(2):183–188.

(67) Myers KP, Olsen CW, Setterquist SF, et al. Are swine workers in the United States at increased risk of infection with zoonotic influenza virus. *Clinical Infectious Diseases*. 2006;42(1):14–20.

(68) Olsen CW, Brammer L, Easterday BC, et al. Serologic evidence of H1 swine influenza virus infection in swine farm residents and employees. *Emerging Infectious Diseases; 2002.8: 8, 814–819.37 ref*. 2002.

(69) Olsen CW, Karasin AI, Carman S, et al. Triple reassortant H3N2 influenza A viruses, Canada, 2005. *Emerging Infectious Diseases*. 2006;12(7):1132–1135.

(70) Ramirez A, Capuano AW, Wellman DA, Lesher KA, Setterquist SF, Gray GC. Preventing zoonotic influenza virus infection. *Emerging infectious diseases*. 2006;12(6):996–1000.

(71) Robinson JL, Lee BE, Patel J, et al. Swine influenza (H3N2) infection in a child and possible community transmission, Canada. *Emerging Infectious Diseases*. 2007;13(12):1865–1870.

(72) Terebuh P, Olsen CW, Wright J, et al. Transmission of influenza A viruses between pigs and people, Iowa, 2002–2004. *Influenza and other Respiratory Viruses*. 2010;4(6):387–396.

(73) Harris RP, Helfand M, Woolf SH, et al. Current methods of the US preventive services task force: A review of the process. *Am J Prev Med*. 2001;20(3 Suppl):21–35.

Appendix A: Summary of Evidence for NACI Recommendation

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO AVIAN POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Alizadeh E (2009)[12]	Cross-sectional seroprevalence	N=152 $n_{exposed}$=127 $n_{control}$=25 Poultry and slaughter-house workers (all men); Controls with regular consumer related poultry exposure (60% females) Iran, Nov 2006	**Avian** H9N2 H7N7	HI assay (WHO protocol), adjusted for potential cross-reactivity between H3 and H9 48 workers (37.7%) were seropositive (titres ≥1:20) Seropositivity in slaughter-house workers was 2.09 times higher than poultry workers (51.6% vs. 24.6%) 83.3% (20/24) evisceration workers were seropositive H7N7 not detected	III	Good
Arzey GG (2012)[13]	Cross-sectional, serological testing	n=7 Symptomatic abattoir workers from a biosecure intensive commercial poultry enterprise experiencing an outbreak of low pathogenic avian influenza A Australia, Mar 2010	**Avian** H10N7	HI assay, MN assay Workers showed signs of conjunctivitis, with 2 reporting rhinorrhea and 1 reporting sore throat Conjunctival swabs collected from 6 workers, nose and throat swabs collected from all workers Partial sequence analysis of samples from two workers confirmed presence of influenza A subtype H10 (similar to subtype H10 chicken isolate) but no virus cultured from workers PPE was not frequently used during the outbreak	III	Good Confirmed H10 in poultry flocks

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO AVIAN POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Bridges CB (2002)[14]	Serological testing with nested case-control analysis	N=1818 n_{worker}=1525 n_{gov}=293 Poultry and government workers involved in poultry culling Hong Kong, 1997–1998	**Avian** A/Duck/Singapore/-Q/F119–3/97 (H5N3)	MN assay with confirmatory Western blot; Seropositive if titres ≥80 10% (n=81) of poultry workers were H5 seropositive with both assays; 29.1% (n=444) of poultry workers were seropositive by MN only Factors statistically associated with being H5 seropositive were the reporting of mortality of >10% of poultry, and butchering poultry 3% (n=9) of government workers were H5 seropositive with both assays; 229 workers gave >1 serum sample and 1 worker seroconverted Being a current smoker was statistically associated with being H5 seropositive (p=.03) in government workers, but not in poultry workers	II–2	Fair Only 1 sample collected from poultry workers, therefore uncertain if seropositivity resulted from current or previous exposure

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO AVIAN POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Cai W (2009)[11]	Cross sectional survey with serological testing	N=97 Firemen, government workers and veterinarians involved in wild bird collection during an outbreak of H5N1 Germany, Feb–Mar 2006 (data collected Mar 2007)	**Human** A/Wisconsin/67/05 (H3N2) A/New Caledonia/20/99 (H1N1) **Avian** A/whooper swan/R65–2/Germany/2006 (H5N1) A/bar-headed goose/Qinghai/1A/2005 (H5N1) A/whooper swan/Mongolia/244/2005 (H5N1)	MN assay, plaque neutralization—reactive if anti-H5 titre ≥1:20; Cross-reactivity to H1N1 and H3N2 assessed 97% reported using at least one PPE during bird collection 7/90 (8%) reported symptoms of acute respiratory disease during the period of bird collection or up to 5 days after (cough, cold, headache, muscle or limb pain) 78/97 (80%) provided serum samples 5 samples reactive against H5 with one sample showing reduced viral replication upon initial test (re-testing at WHO gave negative results); All 5 samples were firemen and showed high antibody-titres against H1N1	III	Fair Study conducted one year after outbreak; May be issues with recall for survey questions, and ability to detect seroconversion as H5 declines quickly Participation was lower among firefighters (55%) compared to other participants (> 80% for government workers and vets)

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO AVIAN POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Ceyhan M (2010)[21]	Survey with serological testing; Paired serum sample collected for HCWs only, one sample for everyone else; Samples tested blindly	N=381 (478 serum samples) n_{cases}=5 n_{family}=28 n_{culler}=95 $n_{asymp\ contact}$=75 $n_{no\ contact}$=81 Individuals affected by outbreak: Surviving cases, family members exposed to cases during infectious period, individuals involved with culling, asymptomatic individuals who contacted diseased chickens in areas with cases, individuals with no known contact with diseased chickens, asymptomatic health care workers (HCWs) in contact with cases Turkey, Feb 2006	**Avian** A/Turkey/13/06 (H5N1) A/Turkey/Turkey/1/2005 (H5N1)	ELISA (positive if absorbance ≥620nm); HI assay (positive if ≥20); MN (positive if titre ≥10) used on samples with antibodies from ELISA or HI, and to test a random sample of negative HI assays Only cases had symptoms suggestive of avian influenza 4 samples found positive by MN (3 cases, 1 family member)	II–3	Fair Laboratory methods not standardized

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO AVIAN POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Dejpichai R (2009)[42]	Cross-sectional seroprevalence survey	N=901 Rural villages where backyard farming is common but have no live poultry markets Thailand, Oct 2005	**Avian** A/Thailand/1(KAN-1)/2004 (H5N1)	MN assay (positive if titres ≥40) confirmed with confirmatory immunoflourescence assay 68.1% of participants reported direct or close contact with backyard poultry 110 participants reported a history of acute respiratory illness: 74.5% reported direct or close contact with backyard poultry, 31.8% reported direct or close contact with sick or dead poultry, 13.6% reported close contact with a person with confirmed H5N1 infection All participants were seronegative for H5N1 neutralizing antibodies	III	Fair Potential for recall bias as survey was conducted for an outbreak that occurred in 2004
Du Ry van Beest Holle, M. (2005)[22]	Survey with serological testing	N=62 (with 25 A/H7N7 index cases) Household members who were exposed to confirmed A/H7N7 index cases (infected poultry workers); People living on poultry farms or keeping backyard poultry were excluded Netherlands, 2003	**Avian** A/H7N7	HI assay (positive if titres ≥1:10) at least 3 weeks after diagnosis of primary case in the household, single sample 8 people (12.9%) reported health complaints (2 met case definition for conjunctivitis only, 4 met case definition of ILI only, and 2 met both definitions) 56/62 provided serum samples and 33 (58.9%) had detectable antibodies against H7 Of 24 households serologically tested, 15 (62.5%) had one or more household contacts with detectable H7 antibodies HI antibodies against A/H7, A/H1, and A/H3 were not cross reactive with the heterologous virus; Neutralisation of A/H7N7 not demonstrated in MN	III	Fair High non-response rate (26.4% of households) with no analysis done to compare responding vs. non-responding households

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO AVIAN POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Gray GC (2008)[43]	Longitudinal survey with serological testing (at baseline, 12 and 24 months)	N=798 $n_{exposed}$=372 $n_{unexposed\ spouses}$=368 $n_{control}$=66 Rural agriculture workers exposed to poultry; unexposed spouses; university controls USA, 2004–2006	**Human** A/New Caledonia/20/99 (H1N1) A/Nanchang/933/95 (H3N2) A/Panama/2007/99 (H3N2) **Avian** A/Duck/Cz/1/56 (H4N6) A/Chucker/ MN/14591–7/98 (H5N2) A/Turkey/MA/65 (H6N2) A/Turkey/ VA/4529/02 (H7N2) A/Turkey/ MN/38391–6/95 (H9N2)	HI (human viruses), MN (avian viruses), RT-PCR; Analysis adjusted for potential cross-reactivity; HI and MN assays started screening at 1:10 dilutions Risk factors associated with elevated MN titres for tested avian strains (workers compared to university controls) : H5—Frequency of contact with poultry (OR: 1.2; 95% CI: 1.02, 15) H6—Working with poultry since 2000 (OR: 3.4; 95% CI: 1.4, 8.5); Chronic medical condition (OR: 5.2, 95% CI: 1.9, 13.9) H7—Hunting wild birds (OR: 2.8; 95% CI: 1.2, 6.5); Working with poultry since 2000 (OR: 2.5; 95% CI: 1.1, 5.7) Elevated antibody against human H1N1 important to H5 and H7 models Only 6/740 (0.8%) and 2/737 (0.3) were found to experience a ≥4 fold rise in antibodies against H5 and H9 respectively during follow-up	II–2	Poor Control group of university participants not adequately matched (younger than exposed) Potential biases could be introduced by voluntary participation, self-reporting of exposure, potential mis-matching between study and circulating viruses, cross-reacting antibodies unaccounted for

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO AVIAN POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Gray GC (2011)[18]	Cross-sectional seroprevalence, age-group matched controls	N=235 $n_{exposed}$=157 $n_{control}$=78 Registered bird banders > 18 years of age and active within the last 12 months; University controls USA, 2009/10	**Human** 4 strains **Avian** 8 strains	HI (human samples; elevated titres considered at ≥1:40), MN (avian samples; elevated titres considered at ≥1:10), RT-PCR Sera collected from 127 (81%) bird banders and 69 (88%) controls 3 bird banders and 1 control had elevated titre against H7N3, H9N2, or H11N3 (AIVs); Bird banders reported banding wild raptors 15% of bird banders reported wearing gloves, 36% used eye protection and 78% washed their hands often or always	III	Fair Groups not completely comparable; Mismatched strains could generate falsely positive results
Hinjoy S (2008)[44]	Cross-sectional seroprevalence survey	N=322 Poultry farmers Thailand, 2004	**Avian** H5N1	MN (positive if ≥80 with confirmatory ELISA or Western blot) No participant was found positive based on cut-off, but 7 (2.2%) had lower reactive antibody titres (4 had titres of 10, 2 had titres of 20 and 1 had titres of 40)	III	Fair Voluntary participation, not comparative analysis done between responders and non-responders
Du Ry van Beest Holle, M. (2010)[45]	Cross-sectional seroprevalence survey (single serum sample)	N=495 Persons working or living on 12 farms from another vaccine effectiveness study Indonesia, Jan–Feb 2007	**Avian** A/Ck/Banten/05–1116/05 (H5N1) A/H5N1/Indo/05/IBCDC-RG	HI (positive: titre ≥160 with 2 independent tests), MN (positive: titre ≥80 with 2 independent tests) One farm experienced an outbreak, but no evidence of antibodies against A/H5N1 was detected 1 individual had a titre of 20 (HI assay), which was inconclusive 55 (11%) complained of fever and cough in the past six months; 17 (3%) reported ILI, with one case exposed to unusual deaths in poultry on the farm	III	Fair Voluntary participation, not comparative analysis done between responders and non-responders

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO AVIAN POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Huo X (2012)[46]	Cross-sectional seroprevalence survey (single serum sample)	N=306 Poultry workers from backyard poultry farms China, Jul–Aug 2010	**Avian** A/Anhui/1/05 A/Hubei/1/10	HI (horse RBC, positive: titre ≥1:160) Overall seropositive rate for H5N1: 2.61% (95% CI: 1.14, 5.09) Seropositive rates were significantly correlated with the medians of increasing poultry number per flock Poultry number per flock was associated with 2.39 (95% CI: 1.00, 5.69) increased risk for seropositive poultry workers adjusted for age and sex	III	Fair Cross-reactivity not considered
Jia N (2009)[47]	Cross-sectional seroprevalence (single serum sample)	N=1467 Farmers and poultry workers in rural villages China, Apr 2006	**Avian** A/African Starling/ England-Q/938/79 (H7N1) A/Chicken/ Shanghai/10/01 (H9N2)	HI (horse RBC, positive: titre ≥1:160) 12 samples were positive for H9, none were positive for H7 No significant association between H9 response and exposure to dead or ill poultry, but 3/4 subjects with highest H9 titres (>1:320) reported exposure to dead or ill poultry at home	III	Fair No standard for HI for H7 or H9, so WHO criteria for H5N1 was used; Only HI used as a serology test; Cross reactivity not accounted for in analysis

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO AVIAN POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Kayali G (2010)[48]	Cross-sectional seroprevalence survey (single serum sample)	N=177 n_{grower}=57 n_{worker}=38 $n_{control}$=82 Turkey growers (backyard and confinement), turkey meat processing plant workers; Unexposed controls USA, Mar 2007–Apr 2008	**Human** A/New Caledonia/20/99 (H1N1) A/Panama/2007/99 (H3N2) **Avian** H4N6 H5N2 H6N2 H7N2 H8N4 H9N2 H11N9	MN (positive at ≥1:10 dilutions, tested in duplicate), HI (guinea pig, positive at ≥1:40, testing for cross-reactivity) 14/95 (15%) exposed had elevated antibody titres against any AIV compared to 7/82 (8.2%) of controls Titres against H5 were higher for growers compared to control (p=.003); when adjusted for H3N2 OR: 4.5 (95% CI: 1.5, 13.3) for being seropositive for H5 No difference in titres for H7 and H11 between groups, but growers (especially small scale) had elevated titres for all other tested subtypes Potential risk factors such as age, gender, smoking, chronic diseases, ILI, use of PPE were not associated with serological outcomes	III	Fair Small numbers; Used low thresholds for assays; Potential for cross-reactivity between AIVs
Kayali G (2011)[49]	Cross-sectional seroprevalence (single serum sample)	N=250 $n_{backyard}$=128 $n_{commercial}$=72 $n_{control}$=50 Chicken growers (backyard and commercial); Urban controls (not exposed to poultry, voluntary) Lebanon, Jul–Sep 2010	**Human** A/Brisbane/59/04 (H1N1) A/California/04/09 (H1N1) A/Brisbane/10/07 (H3N2) **Avian** Subtypes H4-H16	MN (positive at ≥1:10 dilutions, tested in duplicate), HI (horse RBC, testing positive MN samples and for cross-reactivity) Control group had higher titres for seasonal and pandemic H1N1, but groups were similar for H3N2 5 backyard growers tested positive with both MN and HI (3 for H4 and 2 for H11) Commercial growers more likely to use protective equipment	III	Fair Groups not completely comparable

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO AVIAN POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Khuntirat BP (2011)[50]	Cross-sectional seroprevalence	N=800 Villagers ≥20 years of age from rural areas of Thailand affected by highly pathogenic avian influenza (most villagers raise small flocks of domestic poultry e.g. chicken, ducks, quail) Thailand, Apr–Oct 2008	8 Human strains (H1N1, H3N2, H5N1, H9N2) 16 Avian strains (H1N1, H2N2, H4N6, H5N2, H6N1, H6N2, H7N2, H7N7, H8N4, H9N2, H10N4, H10N7, H11N9, H12N5) 2 Swine strains (H1N1, H3N2)	HI (guinea pig or turkey RBC; testing human and swine strains; positive at ≥1:40), MN (testing avian or avian-like strains; positive at ≥1:10) 65.4% participants self-reported poultry exposure (ever being within 1 meter of live poultry for 30 consecutive minutes); less swine exposure (11.4% of participants) 40.2% had elevated titres against A/Env/Hong Kong /MPU3156/2005 (H2N2) but all were born before 1968 suggesting cross-reaction from human pandemic H2N2 30.6% had elevated titre to swine H3N2, but likely due to cross-reactivity with human H3N2 5.6% (n=45) had elevated titres against A/ Thailand/676/2005 (highly pathogenic H5N1), and 3.5% (n=28) against A/ Thailand/384/2006 (highly pathogenic H5N1); infection was not statistically associated with poultry exposure, but not having an indoor water source was a risk factor (OR=3.2, 95% CI: 1.7, 6.1 for 2005 H5N1 and OR=3.1, 95% CI: 1.4, 6.7 for 2006 H5N1) Elevated titre to A/New Caledonia/20/99 (H1N1) was associated with 2005 H5N1 strain (OR=4.2, 95% CI: 1.4, 12.9) 20.4% reported history of heart disease, hypertension or stroke Attempted to control for cross-reactivity in analysis	III	Good

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO AVIAN POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Koopmans M (2004)[51]	Descriptive (Outbreak surveillance)	Population wide N=453 cases reported People who had direct contact with poultry or poultry products that could have been infected with H7, or had close contact with an H7-infected person Netherlands, 2003	**Avian** H7	RT-PCR, HI (turkey RBC; used to type and subtype influenza strains) Most H7 cases detected in poultry cullers (54/131) Attack rate of conjunctivitis = 7.8% Attack rate of ILI = 2% 3 contacts of primary cases had confirmed A/H7 infection, all shared household with a poultry worker or farmer Of contacts of primary cases, conjunctivitis was reported by 70 people, 13 for ILI, and 14 for other illness ILI was reported less often by A/H7 positive cases than people who tested negative Samples positive for A/H7 were highest in first 4 days of illness onset	III	Good
Kwon D (2012)[15]	Descriptive (Outbreak surveillance with serologic testing—single samples from 1576 individuals, paired samples from 936)	N=2512 (3448 samples) Persons working on poultry farms or culled birds during the 2003–04 outbreaks South Korea, 2003/04	**Avian** H5N1	MN (positive if >80, at least 2 independent assays) with confirmatory testing with HI (horse) or H5-specific Western blot 9 MN positive cases (4 single sample, 5 paired samples); 2 positive by HI, but all 9 positive by Western blot; All cullers	III	Good Cross-reactivity not assessed due to limited serum sample

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO AVIAN POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Leibler JH (2011)[52]	Cross-sectional seroprevalence (2 time points)	N=99 $n_{workers}$=24 $n_{control}$=75 Convenience sample of poultry workers and community residents USA, 2003, 2005	**Human** A/New Caledonia/20/99 (H1N1) A/Panama/2007/99 (H3N2) **Avian** A/Duck/Cz/1/56 (H4N6) A/Chucker/MN/14591–7/98 (H5N2) A/Turkey/MA/65 (H6N2) A/Turkey/VA/4529/02 (H7N2) A/Turkey/MN/38391–6/95 (H9N2) A/Chicken/DE/04 (H7N2)	HI (guinea pig), MN (screened at 1:10 dilution) No evidence of infection with any AIVs found High prevalence of H1N1 and H3N2 in both poultry workers and community members	II–3	Fair Convenience sample may have missed individuals who were affected by avian influenza outbreak in 2004

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO AVIAN POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Lu (2008)[53]	Cross-sectional seroprevalence (positive H5N1 cases were followed up for 1 year)	N=1214 $n_{occupational}$=231 $n_{general}$=983 Occupationally exposed (raising, selling and slaughtering of chickens and ducks), and general population (not engaged in activities handling live chickens or ducks) randomly selected from three of nine regions affected by H5N1 outbreaks China, Apr–Jun 2004	**Human** A/New Caledonia/20/99 (H1N1) A/Panama/2007/99 (H3N2) **Avian** A/goose/ Guangdong/1/96 (H5N1) A/African/starling/ Englan-q/983/79 (H7N7) A/chicken/ Shanghi/10/01 (H9N2)	HI (chicken RBC, used for detecting all strains; positive if titres ≥1:20) , MN used to verify a sample of positive HI results (positive if titres ≥1:20) Positive results by HI: H1N1—31.22% (n=379) H3N2—71.75% (n=871) H5N1—2.47% (n=30) H7N7—0.08% (n=1) H9N2—4.86% (n=59) 1 case of H5N1 was still positive one year later (titre 1:40), while all other positive avian cases became negative Positive rate in occupationally exposed was slightly higher for H5N1 (3.03% vs. 2.34%, p>.05), higher for H9N2 (9.52% vs. 3.76%, p<.01), and had the single H7N7 positive case MN assay results were positively correlated with the HI assay results	II–3	Good Cross-reactivity not considered
Ogata T (2008)[54]	Cross-sectional serology (paired sera at least 4 weeks and up to 2 months apart)	N=257 Poultry workers from H5N2-positive chicken farms Japan, Jun–Nov 2005	**Avian** A/Chicken/ Ibaraki/1/2005 (H5N2)	MN (positive if titre 1:40 or greater in paired sera) Adjusted OR for H5N2 positivity in workers over 40 years of age: 4.6 (95% CI: 1.6, 13.7) Adjusted OR for H5N2 positivity in workers with a history of seasonal influenza vaccination: 3.1 (95% CI: 1.6, 6.1) Adjusted for sex, age, number of workers on the farm and/or history of seasonal influenza vaccination	II–3	Fair Time of infection of the farm poultry was unknown; 17% of participants excluded from analysis due to missing data; Use of MN test only may have been insufficient

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO AVIAN POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Ortiz EJ (2007)[55]	Cross-sectional seroprevalence (single serum sample)	N=150 $n_{exposed}$=133 $n_{unexposed}$=17 Poultry farm workers Peru, 2006	**Human** A/New Caledonia/20/99 (H1N1) A/Nanchang/933/95 (H3N2) A/Panama/2007/99 (H3N2) **Avian** 9 subtypes H4–H12	HI (guinea pig RBC) to assess cross-reactivity (dilutions began at 1:10), MN (positive at ≥1:80) Prevalence of AIV low in both groups One poultry-exposed subject had a 1:10 titre against avian H5 and another worker against avian H12	III	Good Study farm had good active surveillance program to corroborate findings
Ortiz JR (2007)[56]	Descriptive seroprevalence survey	N=295 Poultry workers from sites with suspected or confirmed H5N1-affected poultry (farm workers, market workers, cullers), vets from poultry veterinary clinics, laboratory workers from the National Veterinary Research Institute Nigeria, Mar–Apr 2006	**Human** A/New York/55/2005 (H3N2) **Avian** A/chicken/ Nigeria/246/06 (H5N1) A/chicken/ Nigeria/42/2006 (H5N1)	MN assay (positive if titres ≥1:80) with confirmatory HI assay (horse RBC) No significant associations for use of PPE or hand washing among poultry workers No positive samples found in study population for H5N1, but 97% had neutralizing titres ≥1:80 against circulating human H3N2	III	Fair Confirmation of H5N1 infection in poultry was limited; Convenience sample with some effort made to find absent or ill employees
Pawar SD (2012)[57]	Descriptive seroprevalence survey	$N_{workers}$=338 $N_{control\ samples}$=249 Workers from poultry shops and farms; Sera from general population used to establish baseline antibody levels India, Jul–Dec 2010	**Avian** A/chicken/India/ NIV/99321/09 (H9N2)	HI assay (turkey RBC), MN assay; Assay results reported for ≥40, ≥80 and ≥160 cut-offs No positive samples in baseline sera at ≥40 cut-off 21/338 (6.2%) were positive by HI or MN using ≥40 cut-off 4 people by HI and 5 people from MN were positive at ≥80 cut-off; and 2 people and 1 person were positive at ≥160 by HI and MN respectively	III	Good

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO AVIAN POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Puzelli S (2005)[58]	Descriptive serological survey	$N_{serum\ samples}$=983 Workers in several categories of labour in farms Italy, 1999–2003	**Avian** H7N1 H7N3	HI assay (horse RBC) and MN assay, with Western blot or hemagglutinin assay for positive confirmation	III	
Santhia K (2009)[59]	Descriptive household-based cluster seroprevalence survey	N=841 $n_{household}$=291 $n_{market\ vendors}$=87 Poultry rearing households and one live bird market Indonesia, 2005	**Avian** H5N1	HI assay used for poultry (positive if titres ≥20), MN assay used for humans and swine (positive if titres ≥80) Majority of households had chickens and pigs, chickens only, or chickens, ducks and pigs None of chickens or ducks sampled were H5N1 positive by RT-PCR; one duck was positive for an H4 influenza virus None of the surveyed pigs (n=344) were positive for H5N1 by RT-PCR and MN None of the household participants were positive for H5N1 by MN although 57% of participants were in villages with a history of H5N1 outbreaks	III	Fair

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO AVIAN POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Schultsz C (2009)[17]	Descriptive seroprevalence survey	N=500 n_{worker}=183 n_{culler}=317 Poultry workers and cullers Vietnam, 2004–05	**Avian** H5N1	MN assay against 2 sets of influenza strains with positive samples (titres ≥1:80) re-tested by HI (horse RBC; positive if titres ≥1:80); Cross-reactivity with influenza A viruses assessed (four fold or greater reduction of H5 titre in treated sera) None of the workers showed positive titre against H5N1 Small number of cullers were positive in some MN assays, but some samples had suspected H1 cross-reactivity 3 cullers presented with HI titres of 1:20, 1:40 and 1:200; Involved in culling for more than one year	III	Fair
Shafir SC (2012)[19]	Descriptive seroprevalence survey	N=401 Migratory bird handlers USA, 2008–10	**Human** pH1N1 **Avian** 2008 H5N2, H7N2, H9N2 2009 H5N2, H7N3 2010 H5N2, H7N2,	MN assay (positive if titres ≥1:40) Only one individual tested positive for H5N2 No evidence of AIV and pH1N1 co-infection	III	Fair

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO AVIAN POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Vong S (2006)[20]	Descriptive seroprevalence survey	$N_{households}$=93 (351 participants) Rural village with death due to confirmed H5N1 Cambodia, 2005	**Avian** H5N1	RT-PCR, MN assay (positive if titre ≥80) with confirmatory Western blot None of the participants reported having febrile or respiratory illness during the affected period, and none tested positive for H5N1 despite regular, high-intensity contact with poultry or pigs in the majority of the population Slaughtering chickens were not a significant risk factor after controlling for exposures found significant in multivariate analysis (e.g. cleaning up cages/stalls, handling live poultry, purchasing live poultry, cleaning up poultry feathers)	III	Fair Potential for recall bias; cannot assess degree of misclassification without confirmation of H5N1 virus infection in poultry
Wang M (2009)[60]	Descriptive seroprevalence survey	N=2191 Healthy persons from several workplaces (poultry retailers, poultry wholesalers, workers in large-scale poultry-breeding enterprise, farmers in small-scale rural poultry farm, workers in pig-breeding enterprise, retailers of goods other than poultry in food market, general population) China, Mar 2007–Jul 2008	**Avian** H5N1 H5N2 H9N2	HI assay, MN assay; Conditions for positive titre not identified 0.2% and 4.5% prevalence of anti-H5 and anti-H9 antibodies, respectively, in the study population All anti-H5 positive persons with poultry retailers or wholesalers; anti-H9 positive persons found in all study groups Positive rate in anti-H5 lower than anti-H9 among poultry retailers (0.8% vs. 15.5%, p<.001) and wholesalers (0.8% vs. 6.6%, p=.001)	III	Fair

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO AVIAN POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Yamazaki Y (2009)[61]	Descriptive seroprevalence survey	N=266 $n_{outbreak\ region}$=114 $n_{general\ pop}$=100 n_{worker}=52 General inhabitants in region where H5N2 outbreak occurred, general population in Japan, Employees in or were in the poultry industry or related jobs Japan, May–Aug 2006	**Avian** H5N2	MN assay (positive if titres ≥1:40), HI assay (horse RBC; positive if titres ≥1:40) 8 samples from outbreak region, 4 from general population, 8 from poultry workers showed MN titre ≥40 9 samples from outbreak region, 2 from general population, 2 from poultry workers showed HI titre ≥40 Seropositivity was related to age in poultry workers (p=.038) Positives in poultry workers statistically significant compared to general population (p=.018)	III	Good

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO SWINE POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Ayora-Talavera G, (2005)[62]	Serological testing Convenience sample (any resident who visited the health service for any medical condition and required laboratory rests)	N=115 Indigenous Mayan persons from a rural agricultural community (pigs roam freely in town and in and out of houses) Mexico, 2000	**Human** A/Bayern/7/95 (H1N1) A/Sydney/5/97 (H3N2) **Swine** A/Swine/Wisconsin/238/97 (H1N1) A/Swine/Minnesota/593/99 (reassortant H3N2)	HI (chicken RBC; positive when titre ≥1:40) Relative risk of being seropositive from exposure to pigs: human H1—1.93 (1.2, 3.0) human H3—0.88 (0.55, 1.4) swine H1—0.6 (0.08, 4.2) swine H3—1.0 (0.62, 1.6) Reactivity rates were high to H3 subtype influenza viruses, and highest for A/Sw/Minnesota	III	Fair Prevalence of infection in swine unknown
Beaudoin A (2010)[36]	Descriptive survey with serological testing	N=27 $n_{exposed}$=16 $n_{unexposed}$=9 Employees from two large, comparable swine farms (farm swine influenza history known); Exposed individuals were those working on the farm with H2-positive pigs Sep–Dec 2006 USA, 2008	**Human** A/New Caledonia/20/99 (H1N1) A/Panama/2007/99 (H3N2) **Swine** A/Sw/MO/4296424/2006 (H2N3)	HI (CDC protocol; positive if titres ≥1:40; assessed cross-reactivity with H1 and H3 human strains); MN (positive if titres ≥1:40) Four participants were H2N3 positive (three born before 1968, 1 birth year unknown), with only one being part of the exposed group (born in 1949 and seropositivity may be unrelated to recent exposure) All workers reported use of some form of PPE (e.g. boots, masks, gloves, protective clothing), but not associated with likelihood of seropositivity	II–2	Good Small numbers; History of influenza infection in swine known
Gerloff NA (2011)[26]	Serological testing	N=211 $N_{control\ samples}$=224 Healthy individuals with past or present professional exposure to swine; Serum from the general population collected for routine testing used as control Luxembourg, 2009	**Human** A/Luxembourg/43/2009 (pH1N1) A/Luxembourg/572/2008 (Seasonal H1N1) **Swine** A/Swine/Belgium/1/98 (avian-like H1N1 SIV)	MN (WHO protocol; screening from ≥1:10) GMTs significantly higher for swine workers than controls for pandemic virus GMTs higher among swine workers than controls for SIV, but not statistically different Being SIV positive increased OR of being positive for pH1N1 by 2.4 (1.3, 4.3) for swine workers; OR increased by 6 (2.9, 12.6) in controls GMTs for seasonal influenza significantly higher for swine workers than controls	III	Good

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO SWINE POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Gray GC (2007)[63]	Prospective study with serological testing	N=803 $n_{AHS\ swine\ exposed}$=707 $n_{AHS\ non\text{-}swine\ exposed}$=80 $n_{uni\ controls}$=79 Swine workers from the Agricultural Health Study cohort; spouses and university participants used as controls USA, 2004–2006	**Human** A/New Caledonia/20/99 (H1N1) A/Panama/2007/99 (H3N2) **Swine** A/swine/WI/238/97 (H1N1) A/swine/WI/R33F/2011 (H1N2)	HI (CDC protocol, guinea pig RBC used for human strains and turkey RBC used for swine strains; positive at titres ≥1:40 considered initially, but spectrum also evaluated) >90% AHS swine-exposed individuals have worked with swine for >10 years At enrollment: Swine-exposed had higher titres against swine influenza subtypes of H1N1 than other groups Compared to university controls, swine-exposed had increased risk for swine H1N1 adjusted OR 54.9 (13.0, 232.6); non-swine exposed had adjusted OR of 28.2 (6.1, 130.1) Serological activity against swine influenza was observed during follow-up period with relatively few cases of self-reported ILI A/Iowa/CEID23/05 isolated from one individual with symptoms	II–2	Poor Voluntary participation; Age a statistically significant factor in analysis, and there is a difference in average age between university controls and other participants

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO SWINE POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Kitikoon P (2011)[64]	Serology testing	N=243 $n_{exposed}$=78 $n_{control}$=60 n_{swine}=85 Farm workers from two commercial farms; Non-exposed controls recruited voluntarily from Blood Centre and hospital; Swine Thailand, 2008/09	**Human** A/Thailand/CU41/06 (seasonal H1N1) A/Nonthaburi/102/09 (pH1N1) **Swine** A/Swine/Thailand/CU-CB1/06 (H1N1) A/Swine/Thailand/Cu-CHK4/09 (H1N2)	HI (chicken RBC for swH1N1, swH1N2, huH1N1; turkey RBC for pH1N1; titres ≥40 considered exposed) 50 and 92% of workers from the two farms had antibodies against SIV circulating on the farm (individuals included farm owners, pig handlers, veterinarians, farm cleaners and office workers) Compared to control group, exposed workers had OR 42.63 (14.65, 124) for elevated antibodies to SIV H1N1 and OR 58 (13.12, 256.3) to SIV H1N2 Pigs from all age groups on both farms were seropositive to both swine strains; no antibodies detected against human strains	III	Fair Volunteer controls may not represent baseline in the general population

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO SWINE POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Krumbholz A (2010)[65]	Prospective study with serological testing	N=236 $n_{slaughterers/inspectors}$=50 $n_{farmers}$=46 n_{vet}=22 $n_{control}$=118 Professionals with occupational exposure to pigs; Non-exposed controls were blood-donors frequency matched by gender and age Germany, Dec 2007–Apr 2009	Nine human and swine strains	HI assay (chicken RBC for all viruses except A/Berlin/1/2003 which used turkey RBC; high titre if ≥80 and/or fourfold increase GMT), MN assay to confirm HI results, influenza virus-specific ELISA Prevalence of antibodies against SIV compared to control: H1N1 Exposed—2/118 (1.7%; 0, 6; p=n.s.) Slaughterers—2/50 (4%; 0.4, 13.8; p=n.s.) Farmers—0/46 (0%; 0, 7.8; p=n.s.) Vets—0/22 (0%; 0, 15.5; p=n.s.) H1N2 Exposed—7/118 (5.9%; 2.4, 11.9; p=.01) Slaughterers—3/50 (6%; 1.2, 16.6; p=.025) Farmers—2/46 (4.3%; 0.5, 14.9; p=.077) Vets—2/22 (9.1%; 1.1, 29.2; p=.024) H3N2 Exposed—16/118 (13.6%; 7.9, 21.1; p<.001) Slaughterers—7/50 (14%; 5.8, 26.8; p<.001) Farmers—4/46 (8.7%; 2.4, 20.8; p=.006) Vets—5/22 (22.7%; 7.8, 45.4; p<.001) Cross-reaction between human and SIV observed in a small number of cases	II–2	Good

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO SWINE POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Lopez-Robles G (2012)[66]	Cross-sectional with serological testing	N=125 $n_{exposed}$=62 $n_{control}$=63 Swine workers from 15 swine commercial farms; Controls from activities unrelated to swine industry Mexico, 2007/08	**Human** A/New Caledonia/20/99 (H1N1) A/Panama/2001/99-like (H3N2) **Swine** A/Swine/England/163266/87 (human lineage segments H3N2) A/Swine/Wisconsin/238/97 (H1N1)	RT-PCR, HI assay (seropositive with titres ≥1:32) Serological evidence of previous exposure to swine and human influenza detected Exposed had greater seroprevalence for SIV , but lower seroprevalence for human influenza than control group 1/62 exposed individuals had both swine and human H1N1; 5/62 had both swine and human H3N2 1 control had swine H3N2 antibodies History of influenza vaccination protective against swine H3N2 (OR=0.05; 0.01, 0.52; p<.05)	III	Fair Unexposed were not randomly selected, is subject to selection bias, and may not be representative of the general population

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO SWINE POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Myers KP (2006)[67]	Cross-sectional seroprevalence	N=352 $n_{farmers}$=111 $n_{processors}$=97 n_{vets}=65 $n_{control}$=79 Swine-exposed (farmers, meat processing workers, vets/vet techs); Control group from university volunteers without occupational exposure to swine USA, 2002–2004	**Human** A/New Caledonia/20/99 (H1N1) A/Panama/2007/99 (H3N2) A/Nanchang/933/95 (H3N2) **Swine** A/Swine/WI/238/97 (H1N1) A/Swine/WI/R33F/01 (H1N2) A/Swine/Minnesota/593/99 (H3N2)	HI assay (CDC protocol; guinea pig RBC for human strains, turkey RBC for swine strains; positive if titres ≥1:40) All exposure groups had high prevalence of antibodies against swine H3N2, but not significantly different from controls Elevated titres against swine H3N2 were associated with having elevated titres against human H3N2 OR in exposed group vs. control group Swine H1N1 Farmer: 35.3 (7.7, 161.8) Meat processing: 6.5 (1.4, 29.5) Vet: 17.8 (3.8, 82.7) OR in exposed group vs. control group Swine H1N2 Farmer: 13.8 (5.4, 35.4) Meat processing: 3 (1.2, 7.3) Vet: 13 (5.3, 31.8) OR in exposed group vs. control group Swine H3N2 Farmer: 0.4 (0.2, 0.8) Meat processing: 1.5 (0.9, 2.6) Vet: 0.8 (0.4, 1.5) Human H1N1 antisera showed some cross-reactivity against swine H1N1 (titre 1:20) and H1N2 (1:80); H3N2 showed high cross-reactivity to swine H3N2 (>1:640)	III	Fair Control group voluntary and may not represent the general population and is not similar to the exposed group by age and sex

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO SWINE POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Olsen CW (2002)[68]	Survey with serological testing	N=76 $N_{control\ samples}$=114 Farmers, farm employees, spouses and children, farm vets; Control serum samples from urban residents USA, Sep 96–Apr 97	**Human** A/Johannesburg/82/96 (H1N1) A/Nanchang/933/95 (H3N2) **Swine** A/Swine/Indiana/1726/88 (H1N1) A/Nebraska/01/92 (zoonotic human isolate of swine H1N1)	HI assay (chicken RBC; fourfold titre rises, titres ≥40 and ≥80 analyzed further) No cross-reactivity detected between human and swine strains Preseason serum samples from 17/74 farm participants were seropositive to either swine virus (15/17 were seropositive to both) vs. 1/114 among controls, p<.001 GMTs to human viruses were not significantly different from control group 3/74 farm participants had four-fold titre increases to either swine virus Factors associated with seropositivity to swine virus: being a farm owner, being part of a farm family, being ≥50 years of age	III	Fair Exposure for urban controls unknown because they were obtained from a serum bank
Olsen CW (2006)[69]	Case report	n=1 Farm worker Canada, 2005	Triple reassortant A/Ontario/RV1273/05	Virus detected during diagnostic workup in worker, but unclear if he had been actively infected Several other influenza A viruses were isolated from swine across Canada (MB, AB, BC, ON), and turkeys Human, swine and turkey viruses found to descend from a single lineage of viruses; also share a human/classical swine/avian triple reassortant genotype with the H3N2 virus detected in swine in the USA in 1998	III	Good

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO SWINE POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Ramirez A (2006)[70]	Cross sectional survey with serological testing	N=128 $n_{exposed}$=49 $n_{control}$=79 Individuals who had worked in a swine confinement facility within the past 12 months; Controls selected from a concurrent study at a university Majority of exposed were males, whereas majority of controls were female USA, 2004/05	N/A	HI assay (guinea pig RBC for human strains, turkey RBC for swine strains; outcomes grouped into titres <10 and >10) Workers who sometimes or never wore gloves were more likely to have elevated titres (HI >10) compared to controls (OR: 30.3; 3.8,243.5), and other workers who wore gloves most of the time or always (OR: 12.7; 1.1, 151.1)	III	Fair
Robinson JL (2007)[71]	Survey with serological testing	N=54 Members of a communal farm where an infant was hospitalized with a swine-related influenza virus Canada, 2006	**Human** A/New Caledonia/20/99 (H1N1) A/Wisconsin/67/2005 (H3N2) **Swine** A/Ontario/ RV1273/2005 (swine H3N2) A/Canada/1158/2006 (detected in infant)	HI assay (guinea pig RBC; positive at titre ≥32), RT-PCR 8 other members from 3 households were seropositive (HI ≥32) (4 from household of index patient) Most had no swine exposure or had <1h/week of swine exposure Nasal swabs from 25 grower pigs were negative for SIV 4/10 swine serum samples were positive for H3N2 with 1 sample being seropositive for A/Canada/1158/2006	III	Good

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO SWINE POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
Terebuh P (2010)[72]	Prospective cohort (Swine and human surveillance with serological testing)	$n_{Y1\ workers}$=88 (85% of initial enrollment) $n_{Y2\ workers}$ =76 (78% of initial enrollment) 2 age-matched (within 5y) controls per worker; 210 control samples in y1, 202 samples in y2 Workers from a swine production facility; Controls from two urban centres USA, Sep–May 2002–2004	9 influenza strains (human, swine, triple reassortment)	HI assay (positive at titre ≥1:40); Paired sera collected at beginning and end of study, additional serum sample collected from vaccinated workers 2 weeks after vaccination Majority of workers had worked with pigs for 5+ yrs Year 1 15/42 positive responses from workers met ILI definition, but none positive for influenza by culture 111 swine reported to have displayed ILI signs 52 (59%) seropositive to at least one human virus and 46 (52%) seropositive to at least one swine virus 10 workers seroconverted to one or more SIVs; 8 seroconverted between the pre- and post-vaccination sample, the remaining 2 did not receive vaccine (titre rise from 5–20) Seropositivity to SIV associated with receiving seasonal influenza vaccine (p<.05) in year 1 only	II–2	Good Study periods were aligned with human influenza season with no monitoring over the summer although swine outbreaks still occurred

INDIVIDUALS WITH OCCUPATIONAL EXPOSURE TO SWINE POPULATIONS						
Study	**Study Design**	**Participants**	**Influenza type**	**Key findings**	**Level**	**Quality**
				Year 2 11/32 positive responses from workers met ILI definition; one tested positive for influenza 111 swine reported to have displayed ILI signs 55 (72%) seropositive to at least one human virus and 47 (62%) seropositive to at least one swine virus 29 workers seroconverted to one or more SIVs Swine influenza vaccine needlestick injury occurred in 4 (4%) and 11 (14%) workers in year 1 and year 2 respectively Worker GMTs for three SIVs were significantly higher than controls ($p<.0001$) 20 outbreaks identified in swine, 17 were positive for influenza A by RT-PCR		

LEVELS OF EVIDENCE BASED ON RESEARCH DESIGN

I	Evidence from randomized controlled trial(s).
II–1	Evidence from controlled trial(s) without randomization.
II–2	Evidence from cohort or case-control analytic studies, preferably from more than one centre or research group using clinical outcome measures of vaccine efficacy.
II–3	Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.
III	Opinions of respected authorities, based on clinical experience, descriptive studies and case reports, or reports of expert committees.

QUALITY (INTERNAL VALIDITY) RATING OF EVIDENCE

Good	A study (including meta-analyses or systematic reviews) that meets all design- specific criteria* well.
Fair	A study (including meta-analyses or systematic reviews) that does not meet (or it is not clear that it meets) at least one design-specific criterion* but has no known "fatal flaw".
Poor	A study (including meta-analyses or systematic reviews) that has at least one design-specific* "fatal flaw", or an accumulation of lesser flaws to the extent that the results of the study are not deemed able to inform recommendations.

* General design specific criteria are outlined in Harris et al., 2001.[73]

Appendix B: National seasonal influenza vaccination recommendations for workers occupationally exposed to animals

Country	Organization	Recommendation	Reference
Canada	Public Health Agency of Canada—National Advisory Committee on Immunization (PHAC—NACI)	People in direct contact during culling operations involving poultry infected with avian influenza Direct involvement may be defined as sufficient contact with infected poultry to allow transmission of avian virus to the exposed person. The relevant individuals include those performing the cull, as well as others who may be directly exposed to the avian virus, such as supervising veterinarians and inspectors.	An Advisory Committee Statement (ACS). National Advisory Committee on Immunization (NACI): Statement on Seasonal Influenza Vaccine for 2011–2012
	Canadian Food Inspection Agency (CFIA)	Vaccination for those involved in the food production system for biosecurity. (CFIA uses the NACI statement that all healthy Canadians get the seasonal vaccine as the rationale for producers and their families, farm workers, veterinarians, farm service personnel (including feed truck drivers and vaccination and insemination crews), and other people visiting swine operations to get seasonal vaccine.)	CFIA website on Animal Biosecurity ww.inspection.gc.ca/english/anima/biosec/20111207inde.shtml
Australia	National Health and Medical Research Council, Department of Health and Ageing	People involved in the commercial poultry industry or in culling poultry during confirmed avian influenza activity. Vaccination using the current influenza season vaccine composition is recommended for poultry workers and others in regular close contact with poultry during an avian influenza outbreak. Although routine influenza vaccine does not protect against avian influenza, there is a possibility that a person who was infected at the same time with avian and human strains of influenza virus could allow reassortment of the 2 strains to form a virulent strain that could spread from human to human (ie. initiate a pandemic).	Australian Immunisation Handbook 9th ed. (Last updated 26 March, 2008) www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook-influenza (This recommendation is not made in the 2012 seasonal influenza statement produced by the Australian Technical Advisory Group on Immunisation, although they are authors of the immunisation handbook.)
Hong Kong	Centre for Health Protection, Department of Health—Scientific Committee on Vaccine Preventable Diseases	Poultry Workers: Seasonal influenza vaccination is recommended for poultry workers and persons involved in slaughtering of animals potentially infected with highly pathogenic avian influenza virus for minimizing the risk of re-assortment and eventual emergence of a novel influenza virus with pandemic potential through preventing concomitant infections by the human influenza and avian influenza viruses in humans. Pig Farmers and Pig-slaughtering Industry Personnel: Pig farmers and pig-slaughtering industry personnel are recommended to receive seasonal influenza vaccine to prevent emergence of new influenza A virus in either human or pig hosts.	Recommendations on Seasonal Influenza vaccination for the 2011/12 Season www.chp.gov.hk/files/pdf/recommendations_on_seasonal_influenza_vaccination_for_the_201112_season.pdf

Country	Organization	Recommendation	Reference
United Kingdom	Joint Council on Vaccination and Immunisation (JCVI)	An annual influenza vaccination program for poultry workers was introduced in the 2006/07 season as recommended by the Advisory Committee on Dangerous Pathogens (ACDP). This was reviewed in 2010 where JCVI noted that the implementation of the program was difficult and vaccine uptake in this population was low. Since avian influenza occurred infrequently in the UK and Europe, the risk of reassortment events would be very low. JCVI advised that there was no benefit in continuing routine influenza vaccination in poultry workers beyond the 2010/11 season. ACDP advised JCVI in 2006 and 2009 that there was no need to offer pig workers seasonal influenza vaccination as a precautionary public health measure because of limited evidence showing the role of pigs in transmitting influenza to humans. The risk of reassortment of swine and human influenza viruses was also considered low by the ACDP.	Joint Committee on Vaccination and Immunisation: Draft minutes. 6 October 2010 www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@ab/documents/digitalasset/dh_124596.pdf 17 June 2009 www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@ab/documents/digitalasset/dh_116040.pdf
United States	Centers for Disease Control and Prevention—Advisory Committee on Immunization Practices (CDC—ACIP)	CDC has recommended that persons who are charged with responding to avian influenza among poultry receive seasonal influenza vaccination.	Prevention and control of influenza with vaccines. Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010.
		…influenza vaccination of swine workers—regardless of whether or not they have a high risk condition—is important to reduce the risk of transmitting seasonal influenza viruses from ill people to pigs. Seasonal influenza vaccination of workers might also decrease the potential for people or pigs to become co-infected with both human and swine influenza viruses. Such dual infections could result in genetic reassortment of the two different influenza A viruses and lead to a new influenza A virus that has a different combination of genes, and which could pose significant public health concern.	CDC Interim guidance for workers who are employed at commercial swine farms: Preventing the spread of influenza A viruses www.cdc.gov/flu/swineflu/guidance-commercial-pigs.htm
Germany	German Committee for Biological Agents	…Since 2003, the German Committee for biological agents has recommended seasonal influenza vaccination for people exposed to A/H5N1 infected birds or poultry.	[11]