Evidence-Based Practice Group Answers to Clinical Questions

The Risk of Influenza A (H1N1) Infection Among Workers

A Rapid Review

Bу

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and

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for

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About this report

The Risk of Influenza A (H1N1) Infection Among Workers

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About the Evidence-Based Practice Group

The Evidence-Based Practice Group was established to address the many medical and policy issues that WorkSafeBC officers deal with on a regular basis. Members apply established techniques of critical appraisal and evidence-based review of topics solicited from both WorkSafeBC staff and other interested parties such as surgeons, medical specialists, and rehabilitation providers.

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Objective:

To determine whether or not workers in any occupation are at greater risk of influenza A (H1N1) infection.

Methods:

Search Strategy

A search was conducted on Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to May 13, 2020.

The following terms and search strategy were used to identify analytic epidemiologic studies on H1N1:

- 1. Influenza A Virus, H1N1 Subtype/
- 2. ((influenza adj A adj H1N1) or (swine adj flu) or (swine adj origin adj H1N1) or Influenza A virus subtype H1N1 or (Pandemic adj H1N1 adj "09")).mp.
- 3. or/1-2
- 4. ((occupation or occupational or work or working) and (cause or causation or (risk adj factor) or association or etiology)).mp.
- 5. ((occupation or occupational or work or working) and risk).mp.
- 6. ((occupation or occupational or work or working) and epidemiology).mp.
- 7. ((occupation or occupational or work or working) and (incidence or prevalence or attack rate)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
- 8. Occupational Exposure/
- 9. ((worker* or employee*) and exposure*).mp.
- 10. or/4-9
- 11. 3 and 10
- Case-Control Studies/ or Control Groups/ or Matched-Pair Analysis/ or retrospective studies/ or ((case* adj5 control*) or (case adj3 comparison*) or control group*).ti,ab,kw.
- 13. cohort studies/ or longitudinal studies/ or follow-up studies/ or prospective studies/ or retrospective studies/ or cohort.ti,ab. or longitudinal.ti,ab. or prospective.ti,ab. or retrospective.ti,ab.
- 14. 12 or 13
- 15. 11 and 14

The above search strategy resulted in 73 citations. After screening of titles and abstracts, 32 were deemed potentially relevant, of which 30 were acquired in full text form.^{1–32} A remaining 2 Chinese language papers were requested through InterLibrary Loan at the University of British Columbia but still had not been available by the time this review was completed.^{9,10} After full text screening, 10 articles were deemed relevant and included in this review.^{7,11,14,16,19,24–26,29,30}

Study Characteristics and Results:

Appendix 1 summarizes the characteristics and results of the studies included in this review.

We found 10 articles that had the potential to estimate the relative risk of SARS-CoV infection among workers in comparison to either another group of workers or another control population.^{7,11,14,16,19,24–26,29,30}

Cross-sectional Studies

1. Sandoval 2016

In one smaller cross-sectional study, Sandoval and colleagues surveyed emergency room (ER) and operating room (OR) personnel who had worked during the peak of the H1N1pdm 2009 influenza A outbreak at a university hospital in Santiago, Chile.²⁵ Of 260 invitees, only 117 (45%) agreed to participate. Structured surveys and serum samples were obtained at three weeks after the end of the pandemic period. There were 76 ER and 41 OR workers. ER workers were considered frontline workers who were at higher risk of exposure to H1N1 during the peak period.

Overall, 34 of 117 workers (29.1%) were seropositive by hemagglutination inhibition (HI) assay. Among subgroups, 28 of 76 ER workers (36.8%) were seropositive (had positive HI titers), whereas only 6 of 41 OR workers (14.6%) were seropositive. ER workers exhibited a 3.4-fold greater odds of testing seropositive for H1N1 antibodies compared to OR personnel (unadjusted odds ratio [OR] = 3.40 [CI 95%: 1.27 to 9.10]). After adjusting for pre-pandemic vaccination status, compliance to hand hygiene, and use of clinical masks ER workers exhibited a 4.1-fold greater risk of infection (adjusted OR [aOR] = 4.14 [95% CI: 1.24 to 13.86]).

Given the low participation rate, workers in this study were unlikely to be representative of all health care workers at the hospital. Also, given the crosssectional nature of this study (with measurement of work status and seropositivity status at the same point in time) it was not clear that participants were necessarily seronegative before the study period and then seropositive only after exposure to hospital-related work during the pandemic.

2. Wu 2015

In a large cross-sectional study, Wu et al. "identified and randomly selected" 712 swine industry workers from multiple workplaces in Guangdong, China.²⁹ The original objective was to assess the potential for zoonotic transmission of classic swine influenza virus to humans, however serological testing for H1N1pdm09 (the novel human influenza A virus responsible for the 2009 pandemic) was also conducted. As a control group, 502 blood donors with no occupational exposure to pigs were recruited in the study. Questionnaires were administered by trained interviewers. All participants were asymptomatic at the time of sample collection and none had received vaccines against seasonal or H1N1pdm09 virus.

In comparison to the control group, swine workers had a significantly higher seroprevalence of classic swine H1N1 virus, but not human H1N1pdm09 virus. The seroprevalence of H1N1pdm09 was 8.4% in swine industry workers, and slightly higher at 11.4% in control subjects. After adjusting for age and sex, the odds of having a positive test for H1N1pdm09 was similar between groups (aOR = 0.95 [95% CI: 0.64 to 1.43]).

This study was not conducted during the 2009 H1N1 pandemic, however outside of a pandemic scenario occupational exposure to pigs did not appear to be a significant risk factor for H1N1pdm09 infection.

Case Control Studies

1. Castilla 2012

In a multi-centre study of primary health care patients in Spain, 481 patients with laboratory-confirmed pandemic-related influenza A(H1N1)09 were selected as cases.⁷ Ambulatory patient cases and controls were matched to each other in terms of hospital or primary health care area attended. Hospitalized cases and controls were matched in terms of age, date of consultation and province of residence.

After controlling for additional variables (including number of cohabitants, public transportation habits, vaccination status, hand washing and sanitization habits), "being a health care worker" (HCW) was independently associated with nearly a 3-fold increase in the risk of H1N1 infection (aOR = 2.94 [95% CI: 1.53 to 5.66]). Incidentally, receiving an influenza A(H1N1)09 vaccine was associated with an 87% reduction in the risk of H1N1 infection (aOR = 0.13 [95% CI: 0.04 to 0.48]).

2. Fragazy 2016

In another study of swine industry workers, Fragazy et al. recruited pig industry workers and specialist pig veterinarians as cases.¹¹ Controls were selected from a cohort of participants from an ongoing study on influenza in the community. Controls were matched to cases by age group, geographic region, calendar month in which blood sampling was obtained, and gender.

After adjusting for confounders, pig industry workers had an elevated odds of A(H1N1)pdm09 seropositivity (aOR = 20.4 [95% CI: 2.2 to 186.4], P = 0.007) compared to the community-based control group. The association between A(H1N1)pdm09 seropositivity and occupational swine exposure remained strong after controlling for the possible effect of cross-reactivity with other swine influenza strains (aOR = 15.1 [95% CI: 1.6 to 140), P = 0.017).

3. Lobo 2013

In a relatively small study, Lobo and colleagues compared three groups of HCWs at a tertiary care teaching hospital in Brazil.¹⁹ Cases were defined as HCWs with respiratory symptoms and laboratory-confirmed pandemic 2009 H1N1 influenza infection. Two control groups were assembled: 1) HCWs with influenza symptoms and a negative test for 2009 H1N1 influenza; and 2) asymptomatic HCWs who worked at the same hospital unit and during the same time period as a confirmed case. After adjusting for comorbidity, sex, and exposure to either a co-worker or social contact with respiratory symptoms, "being a physician" was independently associated with an 8.6-fold greater odds of acquiring confirmed pandemic influenza compared to asymptomatic HCW controls (aOR = 8.58 [95% CI: 2.52 to 29.27]).

Exposure to high-risk interventions (e.g., aerosolizing procedures) and failure to use personal protective equipment (PPE) were not documented in this study, however the authors speculated that their study physicians may have been subject to both of these circumstances.

4. Pujo 2015

In a large, well reported study by Pujol et al., 996 ambulatory cases and 720 hospitalized cases of confirmed pandemic influenza (i.e., influenza A[H1N1]pdm09) were identified from multiple primary care centres and hospitals throughout Spain.²⁴ Each of these case groups was compared separately to 1,062 ambulatory control patients who had also attended primary care clinics for conditions other than an influenza-like illness (ILI).

The primary objective of this study was to determine if occupational class (manual workers versus non-manual workers) was a determinant of H1N1 infection in each of the two case groups. After adjusting for age, comorbidity, and influenza vaccination status, the risk of H1N1 infection-related ambulatory cases was no greater for manual workers than for non-manual workers (aOR = 0.97 [95% CI: 0.74 to 1.27]), but for H1N1 infection-related hospitalized cases the risk was 53% higher for manual workers (aOR = 1.53 [95% CI: 1.01 to 2.31]).

Cohort studies

1. Jaeger 2011

Jaeger et al. assembled a small cohort of 78 HCWs who had been exposed to at least one of six early cases of laboratory-confirmed H1N1 infections in Southern California during the 2009 pandemic.¹⁴ Exposure was defined as interaction with an index patient within 6 feet in a health care setting. Health care settings were classified as either inpatient or outpatient; HCWs were classified as either clinical practitioners, allied health workers, or administrative workers.

Baseline and follow-up data were collected however the authors did not report the relative risk of infection between different occupational groups. Therefore, from raw data appearing in Table 2 of the full-text article, we calculated unadjusted relative risks (RR) and 95% confidence intervals (95% CIs) for comparisons between health care settings and between HCW types.

Again, in unadjusted analyses only, workers from inpatient settings were actually 56% *less* likely than workers from outpatient settings to be infected (RR = 0.44 [95% CI: 0.17 to 1.12). In analyses of HCW types, we found no significant differences in the risk of H1N1 infection when comparing clinical practitioners to administrative support staff (RR = 1.26 [95% CI: 1.05 to 152], P = 0.8), or when comparing allied health workers to administrative support staff (RR = 1.24 [95% CI: 1.04 to 1.47], P = 0.3). Again, our own calculations are not adjusted for other underlying risk factors or confounding variables.

2. Kuster 2013

In one large, well reported Canadian study, Kuster and colleagues aimed to determine whether adults working in acute care hospitals were at higher risk than other working adults for influenza.¹⁶ They also wanted to identify risk factors for influenza among HCWs. To these ends, they assessed the risk for influenza among 563 HCWs from acute care hospitals and 169 non-HCWs (personnel working in an office-type environment not associated with the provision of health care). Information about vaccination and medical histories, comorbidities, demographic data and potential work-, school-, and other community-related risk factors for respiratory virus infection were collected through weekly online diaries. If symptoms of acute respiratory or febrile illness occurred, participants self-collected a nasal swab sample, which was then submitted for laboratory-testing for H1N1 influenza.

This was a very well reported study employing a strong prospective cohort design. The criteria for study enrolment, and definitions of cases and controls were clearly stated. A multivariable analysis was conducted to control for underlying confounders.

In a bivariate (unadjusted) analysis, the incidence of influenza was not significantly different between groups (P = 0.28). Additionally, in a subsequent multivariable analysis that controlled for age, sex, vaccination status, and potential conditions for H1N1 exposure (including hand-to-face habits, wearing of prescription eyeglasses, use of reusable water bottles, public transit and socializing habits, and household members), working in an acute care hospital was not associated with an increased risk for influenza infection (aOR = 0.49 [95% CI: 0.19 to 1.27, P = 0.28])

3. Smit 2011

Smit et al. conducted a prospective cohort study involving healthcare personnel from a single hospital in Amsterdam.²⁶ Participants were divided into three different risk groups: 1) a high-risk group comprised of resident physicians, nurses, and doctor's assistants in a separate influenza outpatient clinic; 2) an (average) intermediate-risk group comprised of doctors, nurses, and doctor's assistants from internal medicine, cardiology, and pulmonary diseases outpatient clinics; and 3) a low-risk group with no occupational contact with patients, comprised of pharmaceutical technicians, managers, intermediate care team (ICT) workers, assistants, and secretaries. Weekly self-administered questionnaires were used to document signs and symptoms. Throat swabs were also self-administered and tested weekly. Serum was drawn and tested monthly.

There were 26, 20, and 20 healthcare personnel in the high, intermediate, and low-risk groups, respectively. It is not clear how many workers had been invited but declined to participate.

During the study period, only one participant from the entire cohort tested positive for novel influenza A (H1N1) infection. That one case was a nurse in the high-risk group. This translated into an incidence rate in the high-risk group of 5.7 cases per 1,000 person-weeks (95% CI: 0 to 17 per 1,000 person-weeks). Again, no cases of novel influenza A occurred in the intermediate-risk or low-risk groups. The difference in the incidence rate between groups did not reach any level of statistical significance.

4. Yen 2012

In a study from Taiwan, Yen and colleagues recruited and followed 154 HCWs in a children's hospital in early August 2009 until the late stage of the pandemic in March 2010.³⁰ HCWs were classified as either high-risk or low-risk. The high-risk group included staff members that were anticipated to have direct contact with 2009 pandemic influenza A (H1N1) patients or their respiratory samples from the outset of the study. These personnel were mainly pediatricians, nurses, and medical technicians who directly managed patients or handled clinical respiratory samples in the pediatric emergency, outpatient, or laboratory departments. The low-risk group consisted of staff members whose daily work was expected to involve no direct contact with ILI patients or clinical specimens (mainly other nurses and laboratory technicians).

Throughout the pandemic, ILI patients were tested regularly for influenza A and B viruses. Serum samples were obtained at three different times during the study period. Precautions such as isolation, and use of surgical masks for both patients and HCWs were routinely implemented. Very few HCWs in the study cohort used N95 respirators. Of all HCWs who were eligible, 100% agreed to participate. Only 4 participants (2.5%) were subsequently lost to follow-up.

In unadjusted analyses, unvaccinated high-risk HCWs had a slightly higher chance of having laboratory evidence of 2009 H1N1 influenza infection than the low-risk group (25.0% and 10.0%, respectively), however this difference was not statistically significant (P = 0.087). The authors also showed data for national counts of H1N1 infection and concluded that the moderate infection rate in this cohort (12.0 to 16.7%) was not higher than that for the general population.

An adjusted analysis was conducted on only 90 (60%) of the original 150 participants who were not vaccinated at any time during the study period (i.e., mid-pandemic). In this subgroup of participants, high-risk HCWs ended up being 6.5 times more likely to test positive for serum antibodies (adjusted OR = 6.51 (95% CI: 1.13 to 37.52), P = 0.036), and 3-times more likely to have a positive virological test (on RT-PCR) for pandemic H1N1 (adjusted OR, 3.12; 95% CI, 0.88-11.03; P = 0.077) in comparison to low-risk HCWs. This subgroup analysis must be interpreted cautiously as 57% of the original high-risk HCWs were vaccinated in the middle of the study and were subsequently excluded. As a result, the remaining 43% of high-risk HCWs are unlikely to be representative of the original cohort. "Unvaccinated" status (or so-called "vaccine hesitancy") in particular can be associated with other determinants such as complacency and lower aversion to infection risk. Again, such important determinants were not measured and therefore a potential confounding effect cannot be ruled out from this analysis.

Discussion:

In this rapid review, we found 10 studies that compare either the odds, or the risk, of H1N1 infection between different groups of workers, or between workers and some other control group. The results of these studies varies. However, there are six studies that are generally more thoroughly reported^{14,16,24,26,29,30} and they include four that employ a stronger prospective cohort study design.^{14,16,26,30} Overall, these studies conclude there is no increased risk of infection among workers who are in direct contact with H1N1 patients when compared to other workers not similarly exposed. Although one study in this group showed that seroconversion was 6.5 times more likely, and positive virological testing was 3 times more likely, among unvaccinated HCWs, that part of the study excluded more than half of the original high-risk HCWs without measuring and controlling for potentially important determinants of (and therefore confounders for) being vaccinated. In the meantime, the authors also reported that the overall incidence of infection in this cohort was still not higher than that of the general population.³⁰

The other group of studies consists of four less thoroughly reported ones^{7,11,19,25} and which generally employ weaker cross-sectional and case-control study designs compared to the other six studies. This generally weaker group of studies shows significantly increased risks of H1N1 infection between the following: 1) HCWs compared to non-HCWs;⁷ 2) pig industry workers compared to community-based control subjects;¹¹ 3) hospital physicians compared to non-physician hospital personnel;¹⁹ and 4) ER workers compared to OR workers.²⁵

Based on the limited analytic research currently available, this rapid review generally concludes that there is no strong evidence of a consistent association between workers in a specific occupation and a greater risk of H1N1 infection.

Summary:

- We found only a small number of epidemiological studies that allowed for an estimate of the relative odds, or relative risk, of H1N1 infection, mostly among HCWs in comparison to non-HCW control groups.
- Studies that either utilized a stronger prospective study design or were more thoroughly reported generally conclude that there is no significantly increased risk of H1N1 infection among workers with greater direct exposure to H1N1 patients when compared to workers with less or no direct contact.
- Studies that either utilized a weaker retrospective study design or were less thoroughly reported almost invariably conclude that there is a significantly increased risk of H1N1 infection among HCWs having direct contact with H1N1 patients.
- The level of evidence on this issue is low-to-moderate.
- Based on the limited analytic epidemiologic research currently available, the general conclusion of this rapid review is that there is no consistent association between work within a specific occupation and a greater risk of H1N1 infection.

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Appendix 1: Characteristics and Findings of Included Studies

Author	Study design/features	Primary sample size (analysed)	Country	Study population & setting	Exposure &/or case definition/history	Outcome (H1N1) ascertainment	Intended objective or analysis	Data sources	Worker-related results	Comments
Castilla et al 2012	Case-control	962	Spain	Ambulatory primary health care (PHC) patients enrolled in a larger study of cases with pandemic influenza A(H1N1)09 and matched controls treated by 36 Spanish hospitals or their respective PHC areas between July 2009 and February 2010.	Several exposures compared including whether health care worker or not.	Lab-confirmed reverse transcription– polymerase chain reaction (RT-PCR).	Evaluate risk factors and measures to prevent influenza infection in the community.	After giving written informed consent, cases and controls were interviewed by specifically trained health professionals after completion of structure questionnaire.	In the multivariate conditional logistic regression analysis, the risk of a diagnosis of influenza increased for health care workers ($OR = 2.94$, 95% CI 1.53-5.66) adjusted for sex, age, educational level, pregnancy, smoking, major risk conditions, type of interview and the variables shown in the table. The influenza A(H1N1)09 vaccine had a protective effect ($OR = 0.13$, 95% CI 0.04-0.48).	Risk for HCWs vs non- HCWs: crude OR (95% Cl) = 3.82 (2.36 to 6.16); aOR = 2.94 (1.53 to 5.41), after controlling for # of cohabitants, use of public transportation, and use of preventive measures (including vaccination and hand hygiene).
Fragaszy et al 2016	Case-control	123	UK	UK pig industry workers were frequency-matched on age, region, sampling month, and gender with a community-based comparison group from the Flu Watch study.	Occupational pig exposure.	Haemagglutination inhibition (HI) assay for serology.	To assess whether occupational exposure to pigs is a risk factor for human infection with human and swine-adapted influenza viruses.	Voluntary participation of pig industry workers, pig veterinarians for cases. Participants from the concurrent Flu Watch study – a community- level, household-based cohort study of influenza in England – formed the population comparison group.	Pig industry workers showed evidence of increased odds of A(H1N1)pdm09 seropositivity compared to the comparison group, albeit with wide confidence intervals (Cls), adjusted odds ratio (aOR), and after accounting for possible cross-reactivity with other swine A(H1) viruses (aOR) 25.3, 95% Cl (1.4–536.3), P = 0 028. There was strong evidence that pig industry workers had elevated odds of A(H1N1)pdm09 seropositivity [aOR = 20.4, 95% confidence interval (Cl) (2.2–186.4), P = 0.007] compared to the Flu watch comparator population. Adjusted for Vaccination and seropositivity to classical swine H1N1, swine avian-like H1N1 or swine H1N2: aOR 15.11 (1.64– 139.75), p=0.017.	Pig industry workers had elevated odds of A(H1N1)pdm09 seropositivity aOR = 20.4 ; 95% CI: 2 2–186 4; P = 0 007] compared to the Flu watch comparator (general) population. The association between A(H1N1)pdm09 seropositivity and occupational swine exposure remained strong after controlling for the possible effect of cross-reactivity with other strains [aOR = 15.1, 95% Cl (1 6–140), P = 0 017].

Author	Study	Primary	Country	Study	Exposure &/or	Outcome	Intended	Data sources	Worker-related	Comments
	design/features	sample		population	case	(H1N1)	objective or		results	
		size		& setting	definition/history	ascertainment	analysis			
		(analvsed)		Ũ			•			
Lobo et al 2013	Case-control	274	Brazil	Three groups of HCWs at Hospital das Clínicas (HC), a tertiary care teaching hospital in Brazil with confirmed pandemic influenza infection: HCW with respiratory symptoms with laboratory- confirmed 2009 H1N1 influenza (confirmed cases); symptomatic influenza-negative infection: HCW with respiratory symptoms tested and negative for 2009 H1N1 influenza- (influenza-negative cases); and asymptomatic HCW: HCW without respiratory symptoms who worked at the same unit as a confirmed case during the same period (controls: 2 per confirmed case).	HCW with respiratory symptoms with laboratory- confirmed 2009 H1N1 influenza (confirmed cases); symptomatic influenza-negative influenza-negative for 2009 H1N1 influenza (influenza-negative cases); and asymptomatic HCW: HCW without respiratory symptoms who worked at the same unit as a confirmed case during the same period (controls: 2 per confirmed case).	Lab-confirmed (RT-PCR)	To evaluate factors associated with pandemic influenza among HCWs.	Active surveillance data from HC when HCWs presented respiratory symptoms, a tertiary care teaching hospital, Interviews over telephone or personally.	Comorbidities (odds ratio [OR], 19.05; 95% confidence interval [95% C]: 4.75- 76.41), male sex (OR, 5.11; 95% C]: 18.0-14.46), and being a physician (OR, 8.58; 95% C]: 2.52-29.27) were independent risk factors for pandemic influenza infection among HCWs. Contact with symptomatic co-worker or social contact was protective (OR, 0.11; 95% C]: 0.04-0.29). In terms of professional occupation, medical resident, nurse, nurse technician, student, administrative position were not significant independent risk factors. Workplace location (Emergency room, Intensive care unit, Patient ward), Direct patient care, Work at another hospital, Contact with suspected or confirmed pandemic influenza infection cases at hospital with/without respiratory protection, Contact with suspected or confirmed pandemic influenza infection at another hospital with/without respiratory protection, Contact with suspected or confirmed pandemic influenza infection at home, Contact with co-worker or social contart with suspected or confirmed pandemic influenza infection, Respital with/without respiratory protection, Contact with suspected or confirmed pandemic influenza infection at home, Contact with co-worker or social contart with suspected or confirmed pandemic influenza infection, Received influenza vaccine in 2009, were all not independent risk factors.	Being a physician was independently associated with influenza risk (OR, 8.58; 95% CI: 2.52 to 22/7). This effect was independent of other significant risk factors such as sex, comorbidities, and contact with a co-worker or other social contact with symptoms. The authors speculate that based on other studies, physicians can be especially resistant to adhering to PPE use. Another possibility is that physicians were exposed to aerosol generating procedures, however neither adherence to PPE use nor exposure to high-risk procedures were measured in this study.

design/features sample size population case (H1N1) objective or analysis results ////////////////////////////////////	Higher quality study.
size (analysed) & setting definition/history ascertainment analysis Pujol et al 2015 Case-control 2778 Spain Patients from 36 hospitals and 22 (H3N1)pdm09 was An ambulatory case of A (H3N1)pdm09 was Lab-confirmed (RT-PCR) To analyse the existence of an obtained from hospital ambulatory cases to ambulatory cases to ambulatory cases to When comparing ambulatory cases to ambulatory cases to ambulatory cases to Hig	Higher quality study.
(analysed) Pujol et al Case-control 2778 Spain Patients from 36 An ambulatory case of A Lab-confirmed (RT-PCR) To analyse the Medical variables were When comparing Hig 2015 Dispital s and 22 (H3N1)pdm09 was existence of an obtained from hospital ambulatory cases to	Higher quality study.
Pujol et al Case-control 2778 Spain Patients from 36 An ambulatory case of A Lab-confirmed (RT-PCR) To analyse the Medical variables were When comparing Hig 2015 hospitals and 22 (H1N1)pdm09 was existence of an obtained from hospital ambulatory cases to ambulatory cases to	Higher quality study.
senter hore sone senter hore sone L'Addunin, Regen L'Addunin, Regen Cation la sone Cation la sone Catio	A well-reported case control study with very clear description of case definitions and control selection, and "matching" criteria. Even a sample size calculation was reported. Occupation was registered, coded and classified based on the National Classification of Occupations of 2011 criteria. Hospitalized cases were matched to ambulatory controls by age, date of diagnosis, and province of residence. Ambulatory cases were also matched to hospitalized cases by the same criteria. Occupational social class (manual workers versus non-manual workers) was not associated with increased risk of lab- confirmed influenza A (H1N1) infection but was associated with increased risk of hospitalization for influenza A (H1N1) (aOR = 1:53 [95% C1: 0.01 to 2:31], adjusted for age, comorbidity and vaccination status).
and other as professional	

Author	Study design/features	Primary sample size (analysed)	Country	Study population & setting	Exposure &/or case definition/history	Outcome (H1N1) ascertainment	Intended objective or analysis	Data sources	Worker-related results	Comments
								technical support, athletes and artists; (3)Middle occupations (administrative employees and professional support for administrative and other management services); (4) Self-employed; (5) Supervisors and workers in skilled technical occupations; (6) Workers qualified at the primary sector and other workers semi-skilled; and (7) Unskilled workers. These seven categories can be aggregated into six-, five-, three- and two- category classifications [14]. The two-category scheme aggregates categories (1)–(3) in a new category called non- manual workers, and categories (4)–(7) in a manual workers category.		
Sandoval et al 2016	Cross-sectional	117 participants (260 invited)	Chile	Health personnel that worked in the emergency room (ER) and the operating room (OR) in a University Hospital in Chile during at least 3 weeks after the end of the pandemic period (beginning in the last week of November of 2009).	Individuals that worked during the peak of the H1N1pdm2009 Influenza A virus outbreak our University Clinical Hospital, which occurred between epidemiologic weeks 20 to 33 (May to August of 2009).	Haemagglutination inhibition (HI) assay for serology.	To estimate and compare the rate of exposure of high versus low-risk health personnel to 2009 pandemic H1N1 (H1N1pdm2009) influenza A virus in a University Hospital in Chile.	Collected data on the following categorical variables: sex, workplace, seropositivity, influenza vaccination (2009 prepandemic trivalent vaccine), hand hygiene, use of clinical mask and occupation on a voluntary basis where all health personnel from the ER and OR were invited to participate in the study. The experiments conducted to assess the reactivity of these human sera against H1N1pdm2009 were performed in duplicate at the Microbiology Department at Icahn School of Medicine at Mount Sinai, New York.	The samples included 117 individuals, 76 of them worked at the ER (65.0%) and 41 at the OR. Of the total number of the subjects tested, 34/117 (29.1%) were seropositive by HI assay. Of these, 36.8% (28/76) of the workers at the ER had positive HI titers, meanwhile only 14.6% (6/41) of the workers at the OR were seropositive. Expressed in relative terms, the chance of seropositivity in the ER as compared to the OR was 3.4 times greater (odds ratio 3.40; CI 95%, 1.27–9.10). When adjusting the comparison between these groups by the variables "2009 seasonal influenza vaccination", "hand hygiene" and "clinical mask use", the odds ratio of positive HI titers for pH1N1 2009 increased to 4.1 (adjusted OR 4.14; CI 95%, 1.24–13.86) between the	Framed as a prospective study but no follow-up measurements, therefore a cross- sectional seroprevalence study and not a cohort study. Reported odds ratios are really prevalence ratios (PRs). As less than half of all invitees participated, potential self-selection bias is a concern. Only 1 physician, and mostly nurses and paramedics in OR group. By comparison, physicians made up 20 (27%) of participants in the ER group. Only a 45% (117 of 260) participation rate. At ≥ 3 weeks after the end of the 2009 pandemic in Chile, ER workers were 4-times more likely to be

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Author	Study	Primary	Country	Study	Exposure &/or	Outcome	Intended	Data sources	Worker-related	Comments
	design/features	sample		population	case	(H1N1)	objective or		results	
		size		& setting	definition/history	ascertainment	analysis			
		(analysed)								
									staff members of ER versus OR.	seropositive for influenza A (H1N1) than operating room health personnel
									Seropositivity Distribution of OR and ER personnel according to their occupation (OR (Number (%) / Seropositive (%))// Emergency Room (Number (%) / Seropositive (%)) Nurse: 10 (24.4) / $0//22$ (29.7) / 8 (10.8%) Paramedic: 21 (51.2) / 3 (7.3%) //14 (18.9) / 4 (5.4%) Theater Nurse: 5 (12.2) / 1 (2.4%) // - / 0 Janitor: 2 (4.9) / 1 (2.4%) // 7 (9.5) / 4 (5.4%) Clerk: 2 (4.9) / 1 (2.4%) // 8 (10.8) / 3 (4.0%) Physician: 1 (2.4) / 0 // 20 (27.0) / 7 (9.5%) Security Guard: - / $0//3$ (4.1) / 2 (2.7%) N/A: - / / 2 / 0.	(aPR = 4.14 [95% Cl: 1.24 to 13.86] adjusted for significant risks factors = vaccination status, handwashing and use of masks)
Wu et al 2015	Cross-sectional	1214	China	Swine workers from Guangdong province, Southern China including swine keepers, pork processer and quarantine officials were identified and selected randomly between Apr 2013 and May 2014. The exposed group consisted of 712 participants from four types of occupations. Of these, 126 (17.7%) were swine keepers, 169 (23.7%) were pork processer (including pig butchers and pork retailers), 360 (50.6%) were retailers of goods other than pork in food market and 57 (8.0%) were		HI assay for serology.	To assess the potential transmission for zoonotic influenza, sero-antibodies against two kinds of influenza viruses— classical swine H1N1 and human H1N1pdm09 virus were detected in persons whose profession involved contact with swine in Guangdong province, China and compared to a nonexposed control group.	Seroepidemiology study in Guangdong province, Southern China. Serum samples from participants were collected between Apr 2013 and May 2014. Survey questionnaire was completed by trained information on the subject's age, gender, and the nature of their contact with pigs.	Seropositive rate to 2009 pandemic H1N1 virus among swine workers was similar with controls after adjusting for sex and age, aOR 0.95 (0.64–1.43) for the exposed population vs non- exposed controls. The serology numbers by worker type were Swine keepers 10 (7.9), Pork processer 17 (10.1), Retailers of goods other than pork 36 (10.0), Quarantine officials 3 (5.3). Compared to quarantine officials, swinekeepers 0.88 (0.40–1.91), Pork processers 1.36 (0.73–2.53), and retailers of goods other than pork 0.86 (0.29–2.55) were not at greater risk of testing positive for serology of H1N1 (unadjusted OR).	Participants appeared to be selected and enrolled based first on exposure status. Therefore, this study had the potential for being a prospective cohort study. However outcome was only measured once (therefore no longitudinal data) making this a cross- sectional study. Control subjects were described simply as blood donors with no occupational exposure to pigs. No description of how selection bias was mitigated. Controls were younger than cases. No other information measured or provide about baseline risk factors. Prevalence of positive HINI serology among swine workers was similar to controls after adjusting for sex and age, aOR 0.95 (0.64– 1.43).

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				Control group consists of blood donors who had no occupational exposure to pigs were recruited in the study between Apr 2013 and May 2014.						
Jaeger et al 2011	Prospective cohort	78 (63 analysed)	US	HCWs exposed to at least 1 of 6 index patients) experiencing laboratory- confirmed H1N1 infection in Southern California.	Defined as interaction with an index patient within 6 feet within a health care setting. Stratified by health care setting (inpatient vs outpatient) and hospital role (clinical practitioners vs allied health vs administrative).	RT-PCR	To measure patient-to- HCW transmission (and evaluate early PPE use), as well as assess N95 fit testing and influenza vaccination among HCWs during initial phase of outbreak.	Review of medical records and staffing lists to identify all HCWs involved in care of index patients. Standardized questionnaires administered at baseline and follow-up 2 weeks later.	Calculated relative risks (RR) (95% C) from raw data in Table 2 of article: Inpatient worker vs Outpatient workers: 0.44 (0.17 to 1.12), P = 0.02 (i.e., inpatient workers were 56% <i>less</i> likely to be infected). However, no significant differences in risk were found when comparing clinical workers and support staff (RR = 1.26 [95% C]: 1.05 to 152], P = 0.8), or allied health workers and support staff (RR = 1.24 [95% C]: 1.04 to 1.47], P = 0.3). Of 139 potentially exposed HCWs, only 78 (56%) agreed to participate and fill out baseline questionnaire. No data on the 44% non- responders. Final analysis included only 63 of original 139 potentially exposed (9 were excluded on determination they were > 6 feet away from index patient), and only 9 (a small number of) cases.	
Kuster et al 2013	Prospective cohort	732	Canada	18–75 years of age and either worked >8 hours per week in 1 of 5 acute care hospitals (HCW) or in an office-based setting in Toronto (non-HCW) enrolled during May 29– September 27, 2009.	Self-reported responses to online questionnaire. The first and second waves of the influenza pandemic in Ontario were defined as the periods for which the weekly proportion of respiratory specimens that were positive for A(H1N1) pdm09 was >5%, as reported by the Ontario Agency for Health Protection and Promotion.	Web-based diaries from enrollment until March 31, 2010, detailing respiratory symptoms and acute respiratory illness (ARI). Those with ARI were lab-confirmed via RT-PCR.	To assess risk factors for influenza among HCWs and to determine whether, during the first 2 waves of influenza A(H1N1)pdm09, HCWs working in acute care hospitals were at higher risk than non- HCWs for symptomatic influenza.	Influenza Cohort Study, initiated by the Working Adult Influenza Cohort Study Group study. Web-based questionnaire detailing influenza vaccination history, underlying medical conditions, demographic data, potential work- or school-related risk factors for respiratory virus infection, and potential community risk factors.	Influenza infection was associated with contact with family members who had acute respiratory illnesses (aOR: 6.9, 95% CI 2.2–21.8); performing aerosol-generating medical procedures (aOR 2.0, 95% CI 1.1–3.5); and low self- reported adherence to hand hygiene recommendations (aOR 0.9, 95% CI 0.7–1.0) after adjusting for A(H1N1)pdm09 vaccination	Higher quality prospective cohort study with well-defined inception point, case definition, control population and multivariable analysis. In a bivariate analysis (unadjusted), the incidence of influenza was not significantly different between groups (P = 0.28). In a

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				Non-HCWs were intended to provide a sample of working adults at low occupational risk for influenza, so as to bias the study toward the ability to identify an occupational risk in health care.	Aerosol-generating medical procedures were defined as any of the following: administration of nebulized therapy or humidified oxygen at >40%, use of bag-valve mask, manual ventilation, noninvasive ventilation, noninvasive ventilation, open airway suctioning, bronchoscopy or other upper airway endoscopy, tracheostomy, endotracheal intubation, cardiopulmonary resuscitation, oscillatory ventilator, or any procedure that involved manipulation of open ventilator tubing in a mechanically ventilated patient or sputum induction or other deliberate induction of coughing. Adherence to hand hygiene and facial protection recommendations were defined as the self- reported proportion of situations during which hand hygiene and facial protection were performed according to infection control recommendations. Symptomatic influenza influenza-positive PCR results for a participant- collected mid-turbinate				history and community influenza activity. Workers in acute care hospital as a risk factor was not significantly associated with influenza infection (aOR 0.47, 95% CI 0.17– 1.32, p=0.28). Contact with persons with acute respiratory illness, rather than workplace, was associated with influenza infection. Compared with other HCWs, those with symptomatic influenza infection were more likely to be present during aerosol-generating medical procedures >1x per week (38.5% vs. 12.7%; p = 0.02) and reported lower adherence to hand hygiene recommendations (77.5% vs. 95%; p = 0.02). After adjustment for changing risks for influenza infection over time, risk factors for influenza infection among HCWs were: contact with a family member with ARI in the previous week 7.86 (2.20– 28.04), performing or assisting with aerosol- generating medical procedures 1.95 (1.10– 3.48), and lower adherence to hand hygiene recommendations 0.86 (0.74–0.99).	multivariable analysis, there was no association between working in an acute care hospital and risk for influenza infection after adjusting for age, sex, vaccination status, and potential sources of exposure (aOR = 0.49 [95% CI: 0.19 to 1.27, P = 0.28])
Smit et al 2011	Prospective cohort	66	Netherlands	Healthcare personnel from three different exposure categories at several departments of the Slotervaart Hospital in Amsterdam, the Netherlands from mid-August 2009 until the beginning of 2010.	High-risk group = resident physicians, nurses, & doctor's assistants in separate influenza outpatient clinic; (average) intermediate- risk group = doctors, nurses, and doctor's assistants from internal medicine, cardiology, and pulmonary diseases outpatient clinics; low-risk group = no elevated risk, no occupational contact	Weekly throat swabs were tested using RT- PCR. Monthly serum specimens tested with H1N1-specific hemagglutination- inhibition serologic assay.	To determine incidence rates of novel inXuenza A (H1N1) infection among healthcare personnel with different exposure risks during the 2009 H1N1 pandemic.	Data from a weekly clinical questionnaire from a total of 66 individual healthcare workers were used for this analysis. Throat swabs were collected each week and analyzed by RT- PCR in order to detect the H1N1 virus. Blood was drawn at study enrollment and once monthly thereafter, and serum specimens were	One of 26 high-risk group participants proved H1N1 positive once by RT–PCR. This corresponds to an incidence rate in the high- risk group of 5.7/1,000 person weeks (95% Cl O– 17/1,000). None of the intermediate- and low-risk group participants proved H1N1 positive by RT– PCR. Significant antibody titer rises in convalescent sera were demonstrated in three	Prospective cohort study with repeated monitoring (weekly throat swabs, and blood tests at baseline, then at monthly intervals). Only 1 case of positive lab test for influenza A (H1N1) in the high-risk group. This study demonstrates a low incidence rate of influenza A (H1N1)

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					with (influenza) patients, i.e., pharmaceutical technicians, managers, ICT workers, assistants, & secretaries from clinical pharmacology, ICT, management division and the Human Resources department.			tested with an H1N1- specific hemagglutination- inhibition serologic assay.	participants: one was a confirmation of the case that had proved H1N1 positive by RT–PCR; the others occurred in two asymptomatic participants belonging to the low- and high-risk groups.	infection among healthcare workers during the 2009 H1N1 pandemic in a setting with high hygiene standards. The calculated incidence rate of novel influenza A (H1N1) infection in the high-risk group was 5.7/1,000 (95% CI 0.0– 17) person-weeks. Incidence was null in the intermediate- and low- risk groups. The difference in incidence rate between groups did not reach any level of statistical significance.
Yen et al 2012	Prospective cohort	150	Taiwan	Staff members at a children's hospital.	High-risk group = staff that would come in direct contact with H1N1 patients or their samples in pediatric emergency, outpatient or lab departments; Low-risk group = workers (mainly nurses and lab technicians) with no direct contact with influenza-like illnesses (ILI) patients or specimens.	Seroconversion was defined as having a four- fold or greater increase in Hemagglutination inhibition (HAI) antibody titers between any successive paired sera. Sera drawn/tested at three time points: early, middle, and late phases of 2009 pandemic in Taiwan. Either virological or serological tests. Subjects with positive virological tests, either virus isolation or real time PCR from throat swabs, were defined as virologically confirmed 2009 pandemic influenza A (H1N1) infections. Subjects having seroconversions were defined as having serological evidence of 2009 pandemic influenza A (H1N1) infection.	To probe seroepidemiology of the 2009 pandemic influenza A (H1N1) among HCWs.	Questionnaire information about demographics, history of ILI, vaccination status, PPE usage (mainly masks). Patients reported any new symptoms during the study period.	Unvaccinated high-risk HCWs had slightly higher chance of having laboratory evidence of 2009 H1N1 influenza infection than the low-risk group (25.0 and 10.0%, respectively); this difference was not statistically significant (p = 0.087). Being in the high-risk group was an independent factor associated with final seroconversion [adjusted OR, 6.51; 95% confidence interval (CI), 1.13-37.52; p = 0.036). HCWs with ILI or virologically confirmed 2009 influenza A (H1N1) infection were significantly associated seroconversion. Factors such as baseline anti-H1N1 titer, optimal surgical mask usage or hand hygiene did not significantly correlate with seroconversion in both univariate and multivariate analysis for risk factors of virologically confirmed 2009 influenza A (H1N1) infection in unvaccinated HCWs proved ILI episodes as independently associated with virologically	

Author	Study design/features	Primary sample size	Country	Study population & setting	Exposure &/or case definition/history	Outcome (H1N1) ascertainment	Intended objective or analysis	Data sources	Worker-related results	Comments
		(analysed)								
						Subjects with any of the above were defined as having laboratory evidence of H1N1 infection.			confirmed infection (adjusted OR, 15.10; 95% CI, 2.51-90.85, p = 0.003). The high-risk group exhibited higher chance of virologically confirmed infection (adjusted OR, 3.12; 95% CI, 0.88-11.03; p = 0.077).	
									The infection rate of 2009 pandemic influenza A (H1N1) in HCWs was moderate and not higher than that for the general population. No significant difference in seroconversion rates from first to second sampling (before vaccination) was found between high- and low-risk groups (5.4% versus 1.8% or 0.01)	

Appendix 2: WorkSafeBC - Evidence-Based Practice Group Levels of Evidence (adapted from 1,2,3,4)

1	Evidence from at least 1 properly randomized controlled trial (RCT) or systematic review of RCTs.
2	Evidence from well-designed controlled trials without randomization or systematic reviews of observational studies.
3	Evidence from well-designed cohort or case-control analytic studies, preferably from more than 1 centre or research group.
4	Evidence from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments could also be included here.
5	Opinions of respected authorities, based on clinical experience, descriptive studies or reports of expert committees.

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