Vaccination of Health Care Workers to Protect Patients at Increased Risk for Acute Respiratory Disease

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Health care workers (HCWs) may transmit respiratory infection to patients. We assessed evidence for the effectiveness of vaccinating HCWs to provide indirect protection for patients at risk for severe or complicated disease after acute respiratory infection. We searched electronic health care databases and sources of gray literature by using a predefined strategy. Risk for bias was assessed by using validated tools, and results were synthesized by using a narrative approach. Seventeen of the 12,352 identified citations met the full inclusion criteria, and 3 additional articles were identified from reference or citation tracking. All considered influenza vaccination of HCWs, and most were conducted in long-term residential care settings. Consistency in the direction of effect was observed across several different outcome measures, suggesting a likely protective effect for patients in residential care settings. However, evidence was insufficient for us to confidently extrapolate this to other at-risk patient groups.

Respiratory disease is a leading cause of deaths worldwide, and influenza and pneumococcal infections are major contributors. Certain groups, such as persons ≥65 years of age or with chronic underlying health problems (*1*) are particularly vulnerable to severe respiratory disease and have poorer outcomes after infection than does the general population. These persons are likely to be frequent users of health care facilities, and outbreaks have been described in a range of high-risk environments, including acute care (*2,3*), pulmonary (*4*), and infectious diseases wards (*5*); organ transplant departments (*6*); children's wards (*7,8*); neonatal intensive care units (*9*); and nursing homes (*10,11*). Severe respiratory infections often occur despite high vaccine coverage rates among patients, suggesting that seroconversion is suboptimal (*10*). Although the origin of infection often is difficult to establish, evidence from some outbreaks (*5,7,10–14*) suggests that transmission from HCWs to patients is likely.

It is estimated from previous influenza seasons that ≈20% of HCWs have evidence of infection (*15*), although not necessarily acquired in the workplace. Young healthy adults often have asymptomatic infection, and ≈28%–59% might experience subclinical infection (*15*). Many persons with mild or subclinical illness continue to work while infectious, and even when illness is recognized, virus might be shed before symptom onset. In a randomized controlled trial among health care professionals, Wilde et al. demonstrated that influenza vaccine was 88% efficacious for reducing serologically confirmed influenza A infection and 89% efficacious for reducing serologically confirmed influenza B infection (*16*). Therefore, vaccination of HCWs has been widely recommended to provide direct protection for themselves and indirect protection for their patients (*1,17*).

Despite efforts to encourage influenza vaccination of HCWs, coverage has been historically poor. Recently, ethical arguments for mandatory influenza vaccination have been raised that focus not only on the direct and indirect benefits to staff and patient health but also on the economic consequences. Burls et al. (*18*) suggested that at a cost of £51–£405 (US$85–$675) per life-year saved, mandatory vaccination is likely to be cost-effective. However, evidence for the effectiveness of vaccinating HCWs for protecting vulnerable patients is limited.

Two recent systematic reviews considered the evidence for indirect protection of vulnerable patient groups after staff influenza vaccination (*18,19*). They suggest that vaccination of HCWs might be effective for reducing death and influenza-like illness (ILI) among elderly residents, but we are unaware of comparable data related to other at-risk groups. We aimed to identify and assess further evidence for the effect of vaccinating HCWs on patient groups most vulnerable to severe or complicated respiratory illness.

Methods

The full study protocol is registered with the UK National Institute for Health Research International Prospective Register of Systematic Reviews (www.crd.york.ac.uk/PROSPERO [registration no. CRD420111092]). We searched several electronic health care databases, sources of evidence-based reviews, guidelines, and gray literature in accordance with the specifications of each database (Figure). In addition, we contacted domain experts and vaccine manufacturers to identify unpublished data and undertook citation and reference tracking for all included papers. Thesaurus-indexed and free text terms were defined for the population, intervention, and outcome parameters; peer reviewed; and adapted as necessary for each search engine.

Eligibility criteria were defined a priori as follows:

- Types of study: any experiment, observational study, or systematic review reporting on the effectiveness of vaccination (including influenza or pneumococcal vaccines) of HCWs for protecting patients at higher risk for severe or complicated respiratory infection.

- Types of participants: persons at higher risk for severe or complicated illness as a result of acute respiratory infection (as defined in World Health Organization [*1*] and Advisory Committee on Immunization Practices guidance [*17*]), who have received or are receiving care from an HCW.

- Types of intervention: influenza or pneumococcal vaccination of any worker providing medical, nursing, social, or personal health care (because no uniformly accepted definition of an HCW exists, it

was defined by the peer-reviewed terms specified in the search strategy).

- Types of outcome measure: cases or consultations, death or hospitalization for acute respiratory disease, influenza, ILI, or pneumococcal disease.

Published and unpublished reports from any year that were written in Chinese, English, French, Japanese, Portuguese, Russian, or Spanish were considered. A 3-stage process was used to assess eligibility for inclusion screening first by title, then abstract, and then full text. Two reviewers undertook this in parallel for stages 1 and 2 and independently for stage 3. Consensus was reached by discussion; when reviewers disagreed, a third reviewer was consulted for a final decision. Where multiple reports were identified for the same piece of original research, the most recent peer-reviewed source was selected.

Two reviewers independently extracted data from each included, by using a predefined, piloted template. The risk for bias was assessed by using the Cochrane Collaboration tool (20) for experimental and prospective cohort studies, the Downs and Black tool (21) for other observational studies, and the US Agency for Healthcare Research and Quality (22) domain and element-based evaluation instrument for systematic reviews. Again, consensus was reached by discussion, with engagement of a third reviewer as necessary. No additional information was sought from corresponding authors. Data were synthesized qualitatively

by using a narrative approach in accordance with the framework described by the Economic and Social Research Council and recommended by the University of York Centre for Reviews and Dissemination (23).

Results

Study Selection

We identified 12,352 citations (Figure): 10,713 from health care databases and the remainder from additional sources. Seventeen studies met the inclusion criteria at the full text stage; 3 others were identified from citation or reference tracking. Of these, 14 were primary research articles; 4 were cluster randomized controlled trials (RCTs), and 10 were observational studies. Four of the remaining 6 articles were different versions of a report relating to 1 systematic review, and the other 2 were different versions of a report relating to a second systematic review. One of these systematic reviews (18) provided a qualitative analysis of 2 of the earliest cluster RCTs (24,25), and the other (19) provided a quantitative meta-analysis of all 4 cluster RCTs (24–27) and 1 additional observational study (28). We used the most recent and detailed version of each review published in a peer-reviewed source in this study.

All of the primary studies considered influenza vaccination of HCWs (online Appendix Table 1, wwwnc. cdc.gov/EID/article/18/8/11-1355-TA1.htm); therefore, we
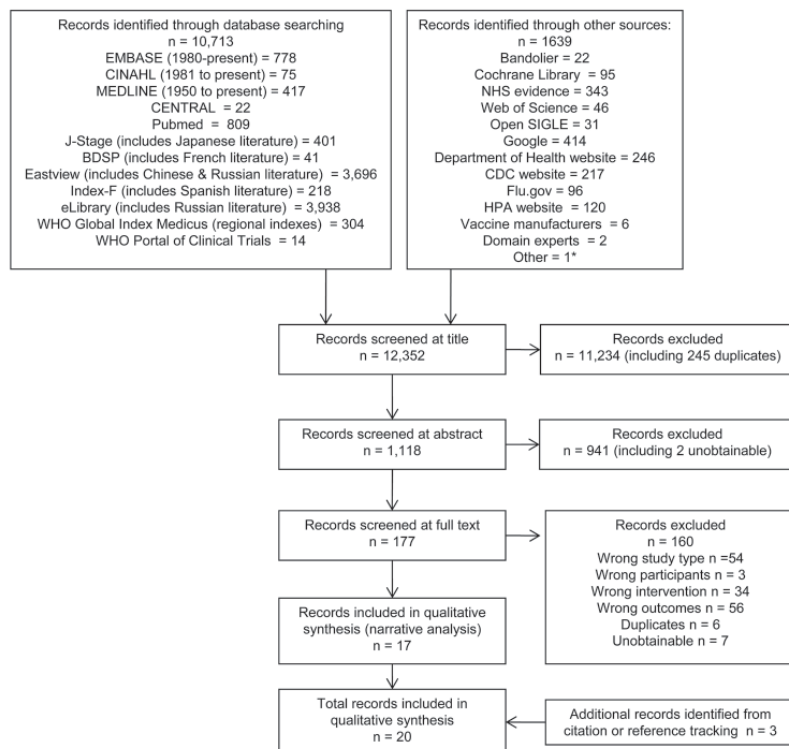

Figure. Study selection for a review of the vaccination of health care workers to protect patients at risk for acute respiratory disease.

Table 1. Risk for bias assessed by using the Cochrane Collaboration tool in a review of the vaccination of health care workers to protect patients at risk for acute respiratory disease*

Study	Sequence generation	Allocation concealment	Blinding of participants, personnel and outcome assessors		Incomplete outcome data		Selective outcome reporting	Other sources of bias
			Primary outcome	Secondary outcomes	Primary outcome	Secondary outcomes		
Lemaitre et al. (26)								
Hayward et al. (27)								
Carman et al. (24)								
Potter et al. (25)								
Saito et al. (33)								
Oshitani et al. (28)								

*Black shading, low risk of bias; light gray shading, uncertain risk of bias; dark gray shading, high risk of bias; blank cells, no secondary outcome measure reported.

discarded our planned subanalysis relating to pneumococcal vaccination. Only 4 studies (24–26,29) defined HCW, even though this definition is likely to affect the probability of transmission and therefore the magnitude of observed effects. Where reported, vaccination among staff ranged from ≈35% to 70% in the intervention arm and from none to 32% in the control arm of experimental studies and from 12% to 90% in observational studies. Eleven of the primary research studies were conducted in long-term care facilities; the remainder were conducted in renal dialysis facilities (30), a pediatric hospital (31), and an adult oncology hospital (32) (1 study each). Where reported, vaccination coverage among patient populations ranged from 0% to ≈90%, and few studies considered additional infection control practices, such as hand washing, duration of contact, or use of face masks, which vary and again influence the propensity for transmission.

Risk for Bias

Cochrane Collaboration Tool

Concerns arose largely from the lack of blinding of participants or study personnel (Table 1). Although the effect was likely to be minimal with regard to the primary outcome for all 4 RCTs (all-cause mortality), it might have resulted in underestimation or overestimation of additional, more subjective, outcome measures, such as incidence of ILI.

All studies, except for that by Lemaitre et al. (26), were judged to be at some further risk for bias. This included

selection bias (inadequate description of selection criteria [24,25,33] or sequence allocation [25,28,33]), performance bias (lack of detail about allocation concealment [25,26]), and measurement bias (no clearly defined outcome measure [28]).

Downs and Black Tool

The Downs and Black tool (Table 2) considers 5 assessment domains, but because most observational studies identified were primarily descriptive, we excluded the power domain in this review. Scores ranged from 3/27 (34) to 10/27 (29,30,35), with higher scores representing lower risk for bias. None of the studies provided sufficient detail about the patient population, and only 1 (29) described principal confounders. Other concerns about reporting related to lack of detail of study objectives (29,32,34), a priori definition of outcome measures (32,34–37) or those lost to follow up (35), failure to provide sufficient detail of statistical analysis (29,30,34–37), lack of randomization or blinding, and failure to adjust outcome measures.

Agency for Healthcare Research and Quality Tool

We assessed the 2 identified systematic reviews (18,19) by using the Agency for Healthcare Research and Quality tool (22). Both appeared to be at a comparatively low risk for bias, providing a clearly defined research question, search strategy, inclusion and exclusion criteria, and description of outcomes. However, details were lacking about blinding of reviewers to authorship and measurement

Table 2. Risk for bias by using the Downs and Black tool in a review of the vaccination of health care workers to protect patients at risk for acute respiratory disease

Study	Type of score (maximum score)*				
	Reporting (11)	External validity (3)	Internal validity, bias (7)	Internal validity, confounding (6)	Total (27)
Ando et al. (30)	5	2	2	1	10
Shugarman et al. (35)	6	0	1	3	10
Kanaoka et al. (29)	5	1	3	1	10
Monto et al. (36)	5	0	2	2	9
Weinstock et al. (32)	4	0	4	1	9
Stevenson et al. (37)	4	1	2	1	8
Munford et al. (34)	2	0	0	1	3

*Maximum score indicates lowest risk of bias for each domain.

Table 3. Cases of and consultations for acute respiratory disease in a review of the vaccination of health care workers to protect patients at risk for acute respiratory disease*

Outcome measure (study)	Study design	Method of assessment	Measure of effect in patient population	Effect estimate (95% CI)
Clinically defined episodes of viral illness (Potter et al. [25])	Cluster RCT	Not defined. No. episodes recorded by study nurses.	OR, nonvaccinated and vaccinated patients	**0.64 (0.48–0.87)**
			OR, vaccinated patients	**0.40 (0.26–0.62)**
			OR, nonvaccinated patients	0.98 (0.65–1.48)
Lower respiratory tract infection				
Potter et al. (25)	Cluster RCT	Defined as 1) pulmonary crackles, wheeze, or tachypnea plus temperature >37.0°C or leukocyte count >10 × 10⁹/L or 2) a positive sputum culture. No. episodes recorded by study nurses.	OR, nonvaccinated and vaccinated patients	0.69 (0.40–1.19)
			OR, vaccinated patients	0.59 (0.25–1.38)
			OR, nonvaccinated patients	0.77 (0.38–1.57)
Thomas et al. (19)	Pooled data		OR, adjusted for clustering	0.71 (0.29–1.71)†

*RCT, randomized controlled trial; OR, odds ratio. **Boldface** indicates statistical significance.
†p = 0.44. p value not reported for other categories.

of agreement in extracting data, which might have resulted in measurement bias.

Synthesis of Results

Cases or Consultations for Acute Respiratory Disease

One RCT reported data (25) for 2 measures of consultation for respiratory disease; episodes of lower respiratory tract infection and suspected viral illness (Table 3). In addition, the estimate for lower respiratory tract infection was adjusted for clustering by Thomas et al. (19). Both measures demonstrated reduced odds, and results were significant for suspected viral illness when vaccinated and nonvaccinated patients were considered together.

The study by Potter et al. (25) was considered to be at a higher risk for bias than the other RCTs identified; thus, the strength of evidence for these outcomes is questionable. In addition, the measures considered are nonspecific, and the observed effects cannot necessarily be attributed to reduced influenza infection. Nasopharyngeal samples were taken

from a subset of patients within 48 hours after symptoms developed; no samples were positive for influenza on immunofluorescence assay.

Cases or Consultations for Influenza or ILI

Data were reported in 13 studies for 5 outcome measures of influenza/ILI. Eight primary studies measured clinically defined influenza/ILI (online Appendix Table 2, wwwnc.cdc.gov/EID/article/18/8/11-1355-TA2.htm; Table 4).

Three RCTs (25–27) measured cases of ILI, and these data were pooled by Thomas et al. (19) to demonstrate a statistically significant reduction in odds. Two observational studies (28,33) also measured cases of clinically defined ILI, demonstrating statistically significant reductions in risk, although the threshold of staff vaccination coverage used to categorize facilities in these studies varied (Oshitani [28] considering facilities where more or fewer than 10 staff were vaccinated, and Saito [33] comparing facilities with ≤40%, 40%–59%, and ≥60% coverage among staff). A third observational study (29) reported no correlation between

Table 4. Clinically defined outbreaks and clusters of ILI in a review of the vaccination of health care workers to protect patients at risk for acute respiratory disease*

Study	Study design	Method of assessment	Measure of effect in patient population	Effect estimate (95% CI)
Oshitani et al. (28)	Prospective cohort	Defined as ILI >10% of total resident population. Mandatory reporting by survey.	OR, unadjusted facilities with ≥10 staff members vaccinated vs. those with <10 staff members vaccinated	**0.30 (0.09–0.69)†**
Stevenson et al. (37)	Cross-sectional	No definition provided. Reporting by survey.	χ² test for trend; logistic regression	χ² p = 0.03; logistic regression p = 0.08
Shugarman et al. (35)	Cross-sectional	Defined as ≥3 residents within a 72-h period with influenza-like symptoms, sudden onset of fever, or "feverishness" and ≥1 of the following respiratory symptoms; sore throat, runny nose, cough, or nasal congestion. Reporting by survey.	OR, facilities with staff vaccination coverage >55% and patient vaccination coverage >89%, vs. those with lower coverage	**0.39 (0.17–0.87)†**

*ILI, influenza-like illness; OR, odds ratio. **Boldface** indicates statistical significance.
†p value not reported.

staff vaccination coverage and cases of influenza in patients, although the relative change in vaccination coverage (79%–91%) was small and thus any difference in the number of cases was probably difficult to detect. The magnitude of reported effects varied, most notably by influenza season in the study of Hayward et al. (*27*), and with patient vaccination status in the study of Potter et al. (*25*).

One study measured general practitioners consultations for ILI (*27*). An inconsistent effect was demonstrated across different periods of influenza activity, but pooled data suggested an overall statistically significant reduction in the odds of consultation after vaccination of HCWs.

Three observational studies (*28,35,37*) demonstrated a statistically significant protective effect of staff vaccination against clinically defined outbreaks of ILI in patients (Table 4). The thresholds used to categorize facilities on the basis of staff vaccination coverage again varied among studies, and these data were considered to be at relatively high risk for bias.

Measures of laboratory-confirmed infection (online Appendix Table 3, wwwnc.cdc.gov/EID/article/18/8/11-1355-TA3.htm) were less frequently reported and generally based on small samples of data at high risk for bias. Five studies measured laboratory-diagnosed influenza (*24,25,31,32,36*), although 1 reported no statistical analysis (*25*). Different methods of defining laboratory confirmation

were used (online Appendix Table 3). Thomas et al. (*19*) pooled data from the 2 RCTs (*24,25*) to demonstrate a small nonsignificant protective effect. This result is supported by evidence from 2 additional observational studies (*31,32*), which indicated a statistically significant reduction in the proportion of laboratory-confirmed cases of nosocomial influenza among inpatient pediatric and oncology patients after implementation of vaccination campaigns. In addition, Monto et al. (*36*) measured outbreaks of laboratory-diagnosed influenza, and this was the only study not to demonstrate a protective effect of vaccinating HCWs. The authors reported a higher, but nonsignificant, median vaccination coverage among staff in homes experiencing outbreaks.

Deaths from Respiratory Infection, ILI, or Acute or Respiratory Disease or Its Complications

Evidence for 5 measures of death was identified (Table 5). All 4 RCTs (*24–27*) considered all-cause death as their primary objective, providing the strongest evidence on the basis of study design. Although not defined a priori as an outcome of interest for this review, data were therefore extracted. These were pooled by Thomas et al. (*19*) to demonstrate a statistically significant protective effect.

Although at higher risk for bias, supporting data were provided for 4 more-specific measures. Thomas et al. (*19*) pooled data from 2 RCTs, 1 measuring deaths after

Table 5. Measures of death in a review of the vaccination of health care workers to protect patients at risk for acute respiratory disease*

Outcome measure and study	Study design	Method of assessment	Measure of effect in patient population	Effect estimate (95% CI), p value
All-cause mortality				
Potter et al. (*25*)	Cluster RCT	Death certificate	OR, vaccinated and nonvaccinated patients	**0.56 (0.40–0.80)†**
			OR, vaccinated patients	**0.57 (0.35–0.91)†**
			OR, nonvaccinated patients	**0.56 (0.34–0.94)†**
Carman et al. (*24*)	Cluster RCT	Not stated	OR	0.62 (0.36–1.04), p = 0.092
Hayward et al. (*27*)	Cluster RCT	Reporting by lead nurse	Rate difference, epidemic period 1	**−0.05 (−0.07 to −0.02)**, p = 0.002
			Rate difference, epidemic period 2	−0.01 (−0.04 to 0.02), p = 0.49
			Rate difference, nonepidemic period 1	0.00 (−0.03 to 0.03), p = 0.93
			Rate difference, nonepidemic period 2	0.01 (−0.03 to 0.04), p = 0.70
Lemaitre et al. (*26*)	Cluster RCT	Not stated	OR	0.86 (0.72–1.02), p = 0.08
Thomas et al. (*19*)	Pooled data		OR, adjusted for clustering	**0.68 (0.55–0.84),** p<0.001
Respiratory deaths: Lemaitre et al. (*26*)	Cluster RCT	Reporting by study nurses	OR	1.55 (0.59–4.10), p = 0.38
Pneumonia-associated deaths				
Potter et al. (*25*)	Cluster RCT	Reporting by lead nurse	OR, vaccinated and nonvaccinated patients	**0.60 (0.37–0.97)†**
			OR, vaccinated patients	0.56 (0.28–1.13)†
			OR, nonvaccinated patients	0.64 (0.33–1.23)†
Thomas et al. (*19*)	Pooled data		Risk ratio, adjusted for clustering	0.87 (0.47–1.64), p = 0.67
Death with influenza-like illness				
Hayward et al. (*27*)	Cluster RCT	Reporting by lead nurse	Rate difference, epidemic period 1	−0.01 (−0.02 to 0.01), p = 0.24
			Rate difference, epidemic period 2	−0.01 (−0.03 to 0.00), p = 0.08
			Rate difference, nonepidemic period 1	−0.01 (−0.04 to 0.02), p = 0.59
			Rate difference, nonepidemic period 2	0.01 (−0.01 to 0.02), p = 0.35
Thomas et al. (*19*)	Pooled data		OR, adjusted for clustering	0.72 (0.31–1.70), p = 0.45
Laboratory-diagnosed influenza at death: Carman et al. (*24*)	Cluster RCT	Nasal swab within 12 h before death	Difference in proportions, influenza positive at death	20%, p = 0.055

*RCT, randomized controlled trial; OR, odds ratio. **Boldface** indicates statistical significance. Shaded fields represent pooled data.
†p value not reported.

Table 6. Measures of hospitalization in a review of the vaccination of health care workers to protect patients at risk for acute respiratory disease*

Outcome measure and study	Study design	Method of assessment	Measure of effect in patient population	Effect estimate (95% CI)
Hospitalization				
Hayward et al. (*27*)	Cluster RCT	Reporting by lead nurse	Rate difference, epidemic period 1	−0.02 (−0.05 to 0.02), p = 0.35
			Rate difference, epidemic period 2	0.00 (−0.03 to 0.04), p = 0.84
			Rate difference, nonepidemic period 1	0.00 (−0.04 to 0.03), p = 0.80
			Rate difference, nonepidemic period 2	0.00 (−0.03 to 0.03), p = 0.86
Lemaitre et al. (*26*)	Cluster RCT	Not stated	OR	1.03 (0.76–1.40), p = 0.85
Thomas et al. (*19*)	Pooled data		OR, adjusted for clustering	0.90 (0.66 to 1.21), p = 0.47
Hospitalization for respiratory causes: Lemaitre et al. (*26*)	Cluster RCT	Not stated	OR	1.01 (0.43–2.34), p = 0.98
Admissions to hospital with influenza-like illness: Hayward et al. (*27*)	Cluster RCT	Reporting by lead nurse	Rate difference, epidemic period 1	**−0.02 (−0.03 to 0.00), p = 0.009**
			Rate difference, epidemic period 2	0.00 (−0.02 to 0.02), p = 0.99
			Rate difference, nonepidemic period 1	−0.01 (−0.02 to 0.01), p = 0.32
			Rate difference, nonepidemic period 2	0.01 (0.00–0.02), p = 0.31

*RCT, randomized controlled trial; OR, odds ratio. **Boldface** indicates statistical significance. Shading indicates pooled data.

pneumonia (*25*), the other measuring respiratory deaths (*26*), and demonstrated a small nonsignificant protective effect. However, the validity of this pooled analysis was questionable because how these outcomes were defined was not clear. Nonsignificant reductions in risk also were observed for laboratory-diagnosed influenza at death (*24*) and death after ILI (*27*). Again, the direction of the observed effects was largely consistent with other measures, providing further support for a hypothesis of indirect protection.

Admission to a Health Care Facility or Any Other Suggestion of Impact

Hospitalization was measured in 2 RCTs (*26,27*), pooled data suggesting a small, nonsignificant effect (Table 6). One RCT also measured hospitalization for respiratory causes (*26*) and 1 admission to hospital with ILI (*27*), although neither demonstrated any apparent effect. This result is particularly noteworthy given the observed decrease in deaths and might reflect health-seeking behaviors.

Discussion

Evidence is limited for the effectiveness of vaccination of HCWs for protecting patients at higher risk for severe or complicated respiratory illness. Despite the broad question posed, extensive searching, and large number of resultant hits, our search resulted in a low yield of studies, all of which focused on influenza with no consideration for pneumococcal infection. This finding is perhaps not surprising because pneumococcal vaccination is not routinely recommended for HCWs and little, if any, evidence exists of nosocomial spread. A consistent direction of effect was observed across multiple outcome measures, with virtually all studies noting a trend toward a protective effect of vaccinating HCWs. This consistency adds to the degree of confidence in interpreting our

overall findings. Given that most studies were carried out in long-term care facilities, we conclude that vaccination of HCWs against influenza is likely to offer protection for this patient group. However, future reviews that specifically examine the effect of vaccinating other outpatient providers, such as home HCWs and hospital staff in acute care, short-stay settings, would clearly be of value. These findings are more difficult to extrapolate to other at-risk groups, although some, albeit limited, evidence was identified from other settings to suggest a similar effect.

The results of all 4 RCTs (*24–27*) and 1 of the observational studies identified (*28*) previously had been pooled in a quantitative meta-analysis (*19*). The authors of this analysis concluded that evidence is lacking that vaccinating HCWs prevents influenza infection in elderly patients because the apparent benefits were confined to nonspecific outcome measures. We considered additional observational data that demonstrate consistency in the direction of the observed effects across specific and nonspecific outcome measures. Although the strength of evidence for more-specific measures is generally much weaker, these findings add greater weight to the hypothesis of a potential protective effect.

The recent position statement by the Society for Healthcare Epidemiology of America (*38*) suggests that further studies are not needed because the biological rationale for vaccination does not vary by practice setting. However, effect size might vary considerably because of patient characteristics and care patterns (staff deployment and duration of inpatient stay), and further evidence is needed among the most at-risk groups where benefits are probably greatest, to enable prioritization of resources, particularly where vaccine shortages or resource limitations might exist.

Previous authors have suggested that vaccination of HCWs might enable development of herd immunity.

Realistically, herd immunity is difficult to achieve in health care settings, especially acute care short-stay settings, because of patient admissions and discharges, visitors, and staff turnover. That said, herd immunity might not be necessary to benefit patients; modeling studies (*39*) suggest a direct association between coverage and attack rates. Such studies (*39*) also suggest variation in the potential for transmission of infection by different staff groups, which should be explored in further detail.

This field of research has some inherent problems. These difficulties result in part from the difficulty of isolating the effect of HCW vaccination, disentangling it from other factors that might influence patient outcomes, such as patient vaccination (as demonstrated by Potter et al. [*25*]) and background influenza activity (as demonstrated by Hayward et al. [*27*]). Staff vaccination itself might be linked to additional confounding variables, such as organizational culture and professional beliefs. In fact, such confounding might explain the difference in findings between the work of Monto (*36*) and the other authors. Prospective collection of information relating to relevant transmission factors and infection control measures that were largely overlooked by the studies in this review should be used to enable appropriate adjustment in future studies. Furthermore, the most appropriate outcome measures are difficult to define because not all persons with laboratory-confirmed infection have symptoms of illness and vice versa. Future studies thus need to demonstrate consistent effects for a range of clearly defined outcomes by using valid measures across several different influenza seasons, with sufficient power to detect true underlying effects.

The findings of our review are subject to several limitations. Because 11 of the 14 primary research articles considered outcomes in long-term care facilities, generalizability to other at-risk groups is limited. In addition, we did not attempt to contact authors of original studies, and the conclusions drawn are limited by the reported detail. Although the number of reviewers was limited as far as possible, some inconsistency might have occurred in the selection, extraction, and assessment of data introducing potential bias, particularly where the opportunity for subjective judgment existed. We attempted to minimize inconsistency by using several standard assessment tools, but their use was limited by lack of information where components were not conducted because of the nature of the study design. Meta-analysis of the 4 RCTs identified had already been conducted, and although we identified additional observational data, the observed heterogeneity limited any further quantitative analysis.

Some wider possible effects of HCW vaccination, such as reduction in absenteeism because of illness, are beyond the scope of this review. Ethically, autonomy needs to be balanced with nonmaleficence, and this need must be addressed when policy decisions about vaccination are considered. Anikeeva et al. (*40*) reported that in a review of 15 studies focusing on the reasons staff accept influenza vaccine, self-protection was the most important. However, patient protection also was perceived as important, particularly among HCWs in settings with higher risk patients (*40*). Nevertheless, HCWs would be justified in claiming that the current evidence base is not especially strong and heavily weighted toward the benefits to patients receiving care in long-term care facilities, although limited evidence would not necessarily legitimize nonacceptance.

The existing evidence base is sufficient to sustain current recommendations for vaccinating HCWs on the grounds that some protection of high-risk patients against influenza seems likely. However, vaccination should be considered 1 element of a broad package of infection prevention and control measures, such as good hand and respiratory hygiene, environmental cleaning, protection against respiratory droplets, and cohorted care during outbreaks. Well-designed studies that strengthen the evidence base might increase compliance with guidelines, resulting in improved coverage.

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