

# Vaccination of healthcare workers to protect patients at increased risk of acute respiratory disease: summary of a systematic review

Gayle P. Dolan,<sup>a</sup> Rebecca C. Harris,<sup>b</sup> Mandy Clarkson,<sup>c</sup> Rachel Sokal,<sup>c</sup> Gemma Morgan,<sup>d</sup> Mitsuru Mukaigawara,<sup>b</sup> Hiroshi Horiuchi,<sup>e</sup> Rachel Hale,<sup>a</sup> Laura Stormont,<sup>b</sup> Laura Bécharde-Evans,<sup>b</sup> Yi-Sheng Chao,<sup>b</sup> Sergey Eremin,<sup>b</sup> Sara Martins,<sup>b</sup> John Tam,<sup>b</sup> Javier Peñalver,<sup>b</sup> Arina Zanuzadana,<sup>f</sup> Jonathan S. Nguyen-Van-Tam<sup>a</sup>

<sup>a</sup>University of Nottingham, Nottingham, UK. <sup>b</sup>World Health Organization, Geneva, Switzerland. <sup>c</sup>NHS Derbyshire County, Chesterfield, UK. <sup>d</sup>Health Protection Agency South West, Gloucester, UK. <sup>e</sup>Tokyo Medical Dental University, Tokyo, Japan. <sup>f</sup>University of Bielefeld, Bielefeld, Germany.  
*Correspondence:* Dr Gayle Dolan, Health Protection Research Group, Division of Epidemiology and Public Health, School of Community Health Sciences, University of Nottingham, Nottingham, UK. E-mail: Gayle.Dolan@hpa.org.uk

Healthcare workers (HCWs) are at increased risk of exposure to respiratory pathogens and may transmit infection to vulnerable patients. This study summarises a recent systematic review, which aimed to assess evidence that influenza or pneumococcal vaccination of HCWs provides indirect protection for those patients most at risk of severe or complicated acute respiratory infection. A number of healthcare databases and sources of grey literature were searched using a predefined strategy, and citations screened for eligibility in accordance with specified inclusion criteria. Risk of bias was assessed using validated tools and results summarised qualitatively. Twenty papers were included in the final review, all of which considered influenza vaccination of HCW. As such, planned

subanalysis of pneumococcal vaccination was discarded. The majority of primary research studies included (11/14) were conducted in long-term care facilities, but there was marked heterogeneity in terms of the population, intervention/exposure and outcomes considered. Consistency in the direction of effect was observed across several different outcome measures, suggesting that influenza vaccination of HCWs is likely to offer some protection. Further evidence is, however, required from acute care settings.

**Keywords** Vaccination, Medical staff, Influenza, Human, Transmission, Patients, Public health.

*Please cite this paper as:* Dolan *et al.* (2013) Vaccination of healthcare workers to protect patients at increased risk of acute respiratory disease: summary of a systematic review. *Influenza and Other Respiratory Viruses* 7(Suppl. 2), 93–96.

## Introduction

Respiratory pathogens cause significant morbidity and mortality, particularly amongst those vulnerable to severe or complicated infection. Evidence-based strategies for the prevention and control of respiratory infection are therefore essential. Healthcare workers are likely to be at increased risk of exposure and may transmit respiratory infections to their patients through the very nature of their work. Indeed, a number of outbreaks of respiratory illness have been described in healthcare settings,<sup>1–10</sup> often involving healthcare workers. Both influenza and pneumococcal infections are important causes of acute respiratory disease and are vaccine preventable. Whilst there is generally considered to be insufficient evidence for the routine use of pneumococcal vaccine amongst healthcare workers, influenza vaccination has been widely recommended.<sup>11,12</sup> Despite efforts to encourage influenza vaccination, however, coverage has been historically poor and ethical arguments for mandatory vaccination have been raised, focusing not only on direct

protection for workers themselves, but indirect protection for those they care for. To date, evidence for the indirect protection of vulnerable groups following either influenza or pneumococcal vaccination of healthcare workers has been uncertain. The following article summarises a recently published systematic review that addresses this issue. The primary manuscript can be accessed for further detail through the following citation: ‘Dolan *et al.* Vaccination of HealthCare Workers to Protect Patients at Increased Risk for Acute Respiratory Disease. *EID* 2012;**18**(8):1225–1234.’

## Methods

Multiple electronic healthcare databases, sources of evidence-based reviews, guidelines and grey literature were searched using a pre-defined, peer-reviewed search strategy. A three-stage process was used to assess eligibility for inclusion, screening citations first by title, then abstract and then full text. Inclusion criteria considered appropriate study design, subject population (patients of all ages at higher risk of severe

or complicated illness as a result of acute respiratory infection), intervention (influenza or pneumococcal vaccination of any person providing health care to higher risk groups), and outcomes (cases or consultations, death or hospitalisation for acute respiratory disease, influenza, influenza-like-illness (ILI) or pneumococcal disease). A number of validated tools were used to assess the risk of bias at outcome level, and data were synthesised qualitatively using a narrative approach.

## Results

A total of 12 352 citations were identified (10 713 from healthcare databases and the remainder from additional sources). No articles considering pneumococcal vaccination were identified, but twenty studies addressing the effect of influenza vaccination of healthcare workers met the inclusion criteria. Fourteen (70%) of the 20 studies were primary research articles (four randomised controlled trials and ten observational studies) and six different reports of two pre-existing systematic reviews. There was marked heterogeneity in the populations, interventions/exposures and outcomes considered. The majority (11/14) of the primary research papers were conducted in long-term residential care settings with the remainder conducted in a renal dialysis facility (1 study);<sup>13</sup> a paediatric hospital (1 study);<sup>14</sup> and an adult oncology hospital (1 study).<sup>15</sup> All identified studies were judged to be at some risk of bias. Table 1 summarises the qualitative synthesis of evidence for each specified outcome measure.

## Conclusion

Since no articles considering pneumococcal vaccination of healthcare workers were identified, findings from this review were restricted to influenza vaccination only. They highlight that evidence for the effectiveness of influenza vaccination of healthcare workers in providing indirect protection for vulnerable groups is limited. Studies were primarily conducted amongst long-term residential care settings, thus presenting challenges for direct extrapolation of the findings to other at risk groups, and to short-stay acute care settings. Two previous systematic reviews<sup>23,28</sup> indicate that influenza vaccination of healthcare workers might be effective in reducing death and ILI amongst residents of elderly care homes, but the authors concluded that evidence was lacking and confined to non-specific outcome measures. This review considers additional observational data and indicates in general, a uniform direction of effect across multiple outcome measures, suggesting that influenza vaccination of healthcare workers is likely to offer some protection to vulnerable patients. Whilst this provides further evidence to support current recommen-

dations for vaccinating healthcare workers against influenza, it should be considered alongside ethical arguments (particularly the balance between autonomy and non-maleficence) when formulating policy decisions. Future well-designed studies that strengthen the existing evidence base (especially amongst other at risk groups and in acute care settings) might, however, encourage compliance with guidelines and result in improved uptake. Studies concerning the effect of pneumococcal vaccine should also be considered. In practice, both influenza and pneumococcal vaccination should be seen as important elements of a broad package of infection prevention and control measures including good hand and respiratory hygiene, environmental cleaning, protection against respiratory droplets and cohorted care during outbreaks.<sup>29,30</sup>

## Acknowledgements

We acknowledge and thank Charles Penn (World Health Organization, Geneva, Switzerland), John Conly (World Health Organization, Geneva, Switzerland), Charles Beck (University of Nottingham, Nottingham, UK), Bruce McKenzie (University of Nottingham, Nottingham, UK) Andrew Hayward (University College London, UK), John Watson (Health Protection Agency, UK), Arnold Monto (Michigan University, USA), Guy Boivin (Laval University, Canada), Scott Halperin (Dalhousie University, Canada) and Herjo Kok (Maastricht University, the Netherlands) for their support and advice throughout the project. We thank European Vaccine Manufacturers, GlaxoSmithKline, Novartis and Sanofi-Pasteur MSD for responding to our request for literature potentially relevant to this systematic review.

## Author contributions

Protocol design: GD, RCH, RH, JSN-V-T; Execution of search strategy & screening: GD, RCH, MM, HH, LB, YC, SE, SM, JT, JP, AZ, RH; Risk of bias assessment & acquisition of data: GD, RCH, MC, RS, GM, MM, HH, LS; Analysis & interpretation of data: GD, JVT; Manuscript preparation: GD, RCH, JSN-V-T; Final manuscript approval: All listed authors have read and approved the final manuscript.

## Funding

This research was commissioned and funded by the World Health Organization (WHO) Global Influenza Programme. The University of Nottingham Health Protection Research Group is an official WHO Collaborating Centre for pandemic influenza and research. It receives limited funding from WHO in support of specific activities.

**Table 1.** Summary of findings by outcome measure

Outcome	Evidence available	Narrative synthesis
Acute respiratory disease	Statistical estimates from one randomised controlled trial <sup>16</sup> providing two different measures of effect (clinical episodes of viral illness/lower respiratory tract infection).	Inconsistent effect but uniform in direction, suggesting possible protection. Difficult to ascertain whether this may be attributable to influenza infection due to the non-specific nature of the measures used.
Clinically defined cases of influenza-like-illness (ILI)	Statistical estimates of clinically defined ILI from three randomised controlled trials <sup>16–18</sup> and two prospective cohort studies. <sup>19,20</sup> Additional statistical estimate of cases of influenza from one cross-sectional study <sup>21</sup> and observational data from two further studies providing no statistical estimates. <sup>13,22</sup>	Pooled data <sup>23</sup> from the three randomised controlled trials suggest a statistically significant protective effect when adjusted for clustering. This is supported by observational data, of which two of the five remaining studies also demonstrate statistically significant reductions in risk, <sup>19,20</sup> although noted to be at higher risk of bias.
GP consultations for ILI	Statistical estimate from one randomised controlled trial. <sup>18</sup>	Inconsistent effect across different seasons. Small, statistically significant reduction in the rate of consultations for one season only, although overall statistically significant, protective effect when converted to an adjusted odds ratio. <sup>23</sup>
Outbreaks/clusters of ILI	Statistical estimates from three observational studies. <sup>20,24,25</sup>	All three studies demonstrate statistically significant, protective effects, although different ILI definitions employed, imprecise estimates and a high risk of bias.
Laboratory diagnosed influenza	Statistical estimates from one randomised controlled trial <sup>26</sup> and two observational studies. <sup>14,15</sup> Observational data, with no statistical analysis from a further randomised controlled trial. <sup>16</sup>	Pooled data from the two RCTs <sup>23</sup> suggest a small non-significant protective effect. Direction of effect supported by data from two additional observation studies <sup>14,15</sup> which demonstrate statistically significant protective effects. Notable risk of bias and imprecision due to very small sample sizes.
Laboratory confirmed outbreaks of influenza	Statistical estimate from one observational study. <sup>27</sup>	No statistically significant difference although vaccination coverage appeared higher in homes experiencing outbreaks. Analyses are, however, unadjusted and imprecise due to small numbers.
Respiratory mortality	Statistical estimates from four randomised controlled trials <sup>16–18,26</sup> although each provides a different measure (deaths associated with pneumonia, <sup>16</sup> respiratory deaths, <sup>17</sup> deaths with ILI <sup>18</sup> and laboratory diagnosed influenza at death. <sup>26</sup> )	Pooled estimates <sup>23</sup> using data for deaths associated with pneumonia <sup>16</sup> and respiratory deaths <sup>17</sup> suggest a small, non-significant protective effect. Small non-significant protective effects for mortality following ILI <sup>18</sup> and mortality due to laboratory confirmed influenza <sup>26</sup> are also demonstrated in individual studies.
All-cause mortality	Statistical estimate from four randomised controlled trials. <sup>16–18,26</sup>	Inconsistent effect, but uniform in direction. Pooled data <sup>23</sup> suggest a statistically significant, protective effect when adjusted for clustering.
Hospitalisation	Statistical estimates from two randomised controlled trials <sup>17,18</sup> providing three different measures of effect (hospitalisation, <sup>17,18</sup> hospitalisation for respiratory causes <sup>17</sup> and admission with ILI. <sup>18</sup> )	No clear effect demonstrated.

## Conflict of interest

The University of Nottingham Health Protection Research Group is currently in receipt of research funds from Glaxo-SmithKline (GSK). The group has recently accepted an unrestricted educational grant for influenza research from F. Hoffmann- La Roche. Research on influenza funded by an unrestricted educational grant from Astra-Zeneca is also underway. JSN-V-T has given a talk on a related topic for

which expenses were paid by the European Society for Clinical Microbiology and Infectious Diseases; he has received speaker honoraria from Sanofi-Pasteur, MSD, F. Hoffmann- La Roche and GSK; and remuneration for consultancy work from Baxter AG, GSK, F. Hoffmann-La Roche, Novartis and Solvay. All such paid consultancy and speaker engagements ceased in September 2010. JSN-V-T is a former employee of SmithKline Beecham, F. Hoffmann-La Roche and Sanofi-Pasteur MSD, all prior to 2005. RH is currently working on a project funded by

Astra-Zeneca, which considers attitudes to the use of intranasal influenza vaccine. RCH serves as a consultant for GlaxoSmithKline (GSK) Vaccines, which began after major contributions to manuscript. GPD has no potential conflicts to declare.

## References

- Weingarten S, Friedlander M, Rascon D, Ault M, Morgan M, Meyer RD. Influenza surveillance in an acute-care hospital. *Arch Intern Med* 1988; 148:113–116.
- Jacomo V, Sartor C, Zandotti C, Atlan-Gepner C, Drancourt M. Nosocomial Influenza outbreak in an intensive-care unit. *Med Mal Infect* 2001; 31:563–568.
- Rivera M, Gonzalez N. An influenza outbreak in a hospital. *Am J Nurs* 1982; 49:1836–1838.
- Horcajada JP, Pumarola T, Martinez JA *et al.* A nosocomial outbreak of influenza during a period without influenza epidemic activity. *Eur Respir J* 2003; 21:303–307.
- Malavaud S. Nosocomial outbreak of influenza virus A (H3N2) infection in a solid organ transplant department. *Transplantation* 2001; 72:535–537.
- Hall CB, Douglas RG. Nosocomial influenza infection as a cause of intercurrent fevers in infants. *Pediatrics* 1975; 55:673–677.
- Lester-Smith D, Zurynski YA, Booy R, Festa MS, Kesson AM, Elliott EJ. The burden of childhood influenza in a tertiary paediatric setting. *Commun Dis Intell* 2009; 33:209–215.
- Meibalane R. Outbreak of influenza in a neonatal intensive care unit. *J Pediatr* 1977; 91:974–976.
- Strausbaugh LJ, Sukumar SR, Joseph CL. Infectious disease outbreaks in nursing homes: an unappreciated hazard for frail elderly persons. *Clin Infect Dis* 2003; 36:870–876.
- Nuorti JP, Butler JC, Crutcher JM *et al.* An outbreak of multidrug-resistant pneumococcal pneumonia and bacteremia among unvaccinated nursing home residents. *N Engl J Med* 1998; 338:1861–1868.
- WHO guidelines for pharmacological management of influenza. Revised February 2010. Part 1: recommendations Available at [http://www.who.int/csr/resources/publications/swineflu/h1n1\\_guidelines\\_pharmaceutical\\_mngt.pdf](http://www.who.int/csr/resources/publications/swineflu/h1n1_guidelines_pharmaceutical_mngt.pdf) (Accessed 10 December 2010).
- Centers for Disease Control Prevention. Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep* 2010; 59:1–5.
- Ando R, Kaname S, Yoshida M. Survey of novel influenza A (H1N1) infection and vaccination in dialysis facilities in the Tokyo Tama area. [in Japanese] *Nihon Toseki Igakki Zasshi* 2010; 43:891–897.
- Engels O, Goldman N, Doyen M, Duyse M, Van Beers D, Vergison A. Reduction of the nosocomial influenza A burden in a paediatric hospital by immunisation of the healthcare workers. Abstract number: 1133\_242, 15th European Congress of Clinical Microbiology and Infectious Diseases, Copenhagen/Denmark, April 2-5, 2005.
- Weinstock DM, Eagan J, Malak SA. Control of influenza A on a bone marrow transplant unit. *Infect Control Hosp Epidemiol* 2000; 21:730–732.
- Potter J, Stott DJ, Roberts MA *et al.* Influenza vaccination of healthcare workers in long-term-care hospitals reduces the mortality of elderly patients. *J Infect Dis* 1997; 175:1–6.
- Lemaitre M, Meret T, Rothan-Tondeur M *et al.* Effect of influenza vaccination of nursing home staff on mortality of residents: a cluster-randomized trial. *J Am Geriatr Soc* 2009; 57:1580–1587.
- Hayward AC, Harling R, Wetten S *et al.* Effectiveness of an influenza vaccine programme for care home staff to prevent death, morbidity, and health service use among residents: cluster randomised controlled trial. *Br Med J* 2006; 333:1241–1242.
- Saito R, Suzuki H, Oshitani H, Sakai T, Seki N, Tanabe N. The effectiveness of influenza vaccine against influenza A (H3N2) virus infections in nursing homes in Niigata, Japan, during the 1998–1999 and 1999–2000 seasons. *Infect Control Hosp Epidemiol* 2002; 23:82–86.
- Oshitani H, Saito R, Seki N. Influenza vaccination levels and influenza like illness in long term care facilities for elderly people during an Influenza A (H3N2) epidemic. *Infect Control Hosp Epidemiol* 2000; 21:728–730.
- Kanaoka S. Inpatient and Personnel Vaccination Influence on Influenza Outbreaks in Long-term Medical and Care Hospital [in Japanese]. *Kansenshogaku Zasshi* 2010; 84:14–18.
- Munford C, Finnigan S. Influenza campaign 2006 and 2007: a residential care success story. *Can J Infect Control* 2008; 23:222–227.
- Thomas RE, Jefferson T, Lasserson TJ. Influenza vaccination for healthcare workers who work with the elderly. *Cochrane Database Syst Rev* 2010; (2):CD005187.
- Stevenson CG, McArthur MA, Naus M, Abraham E, McGeer AJ. Prevention of influenza and pneumococcal pneumonia in Canadian long-term care facilities: how are we doing? *Can Med Assoc J* 2001; 164:1413–1419.
- Shugarman LR, Hales C, Setodji CM, Bardenheier B, Lynn J. The influence of staff and resident immunization rates on influenza-like illness outbreaks in nursing homes. *J Am Med Dir Assoc* 2006; 7:562–567.
- Carman WF, Elder AG, Wallace LA *et al.* Effects of influenza vaccination of health-care workers on mortality of elderly people in long-term care: a randomised controlled trial. *Lancet* 2000; 355:93–97.
- Monto AS, Rotthoff J, Teich E *et al.* Detection and control of influenza outbreaks in well-vaccinated nursing home populations. *Clin Infect Dis* 2004; 39:459–464.
- Burls A, Jordan R, Barton P *et al.* Vaccinating healthcare workers against influenza to protect the vulnerable—Is it a good use of healthcare resources? A systematic review of the evidence and an economic evaluation. *Vaccine* 2006; 24:4212–4221.
- Centers for Disease Control and Prevention. Prevention strategies for seasonal influenza in healthcare settings. Available at <http://www.cdc.gov/flu/professionals/infectioncontrol/healthcaresettings.htm> (Accessed 21 November 2012).
- Health Protection Agency. Infection control precautions to minimise transmission of Respiratory Tract Infections in the healthcare setting, 2011-12. Available at [http://www.hpa.org.uk/webc/HPAwebFile/HPAweb\\_C/1317131892566](http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1317131892566) (Accessed 21 November 2012).