

## **Practical prevention of noscomial influenza transmission, ‘a hierarchical control’ issue**

Frank O’Reilly<sup>a</sup>, Gayle P Dolan<sup>b</sup>, Jonathan Nguyen-Van-Tam<sup>c</sup>, Peter Noone<sup>d</sup>

a An Post, GPO, Dublin, Ireland;

b Field Epidemiology Services, Public Health England;

c University of Nottingham School of Medicine, Nottingham, UK.

d HSE, Dublin Ireland

Seasonal influenza is an important public health issue, with conservative estimates of 25 excess deaths per 100,000 people each season, for a potentially preventable illness.<sup>1</sup> Controlling influenza transmission in healthcare settings is important given greater environmental exposure due to high concentrations of infected patients (some not identified as influenza cases) and possible transmission between health care workers (HCWs) and patients. Healthcare facilities host some of the most vulnerable patient groups at risk of severe or complicated infection, particularly the elderly or those with chronic underlying health problems.<sup>2</sup> Nosocomial outbreaks are described in a number of different healthcare settings<sup>3</sup> and nosocomial attack rates are estimated at around 1 in 200 hospital admissions.<sup>4</sup> Attack rates may be higher and the consequences more severe in high risk settings or within vulnerable populations such as residents of elderly care homes. Indeed those over 65 years account for 90% of influenza-related deaths.<sup>5</sup>

Healthcare organisations have a duty of care to protect both HCWs and patients. Annual immunisation of HCWs is widely recommended by public health as a primary control measure with the dual aims of providing both direct protection for HCWs and indirect protection for their patients.. However, for decades it has been recognised that evidence for the effectiveness of vaccination in providing direct protection of HCWs is limited.<sup>6</sup> Logically it may be expected, given the close contact nature of health care provision, that HCWs are at increased risk of exposure to influenza. Despite this, it has not been established that they are at any greater risk of influenza illness through work. One study suggested that influenza illness in HCWs is more strongly associated with household rather than occupational exposures.<sup>7</sup> While the rate of both symptomatic and asymptomatic influenza in HCWs may be elevated compared with non-health workers, a recent systematic review could not identify from the limited evidence why this occurs and whether it is a direct consequence of health care itself.<sup>8</sup> Recent evidence suggests that in the healthy adult population, vaccination has a very modest effect with an average overall reduction in absence from work of just 0.04 days,<sup>9</sup> but these data do not contradict the evidence that vaccination in HCWs protects vulnerable patients.

There is some evidence, albeit limited, that influenza vaccination of HCWs provides indirect protection to the highly vulnerable residents of elderly care homes. A number of systematic reviews have assessed this evidence,<sup>10-13</sup> the highest quality evidence coming from four cluster randomised controlled trials (RCTs).<sup>14-17</sup> While there is consistency in the direction of effect across several outcome measures, a number of other factors including non-blinding of staff

and differences in vaccination coverage or health status between cases and controls limits causal inference. There are also methodological concerns about the conclusion of these four RCTs. For example, in the study by Potter et al. the divergence in morbidity and mortality preceded the influenza outbreak and was possibly unrelated to influenza<sup>17</sup>. In the studies by Carman and Hayward data on the temporal relationship between influenza and mortality and confounding effects of disability and patient vaccination were not fully controlled for.<sup>14,15</sup> In another study, staff awareness in vaccinated homes may have increased use of general preventive measures effective also against other respiratory viruses such as respiratory syncytial virus (RSV).<sup>16</sup> The reduced morbidity and mortality in the Lemaitre study occurred before the influenza outbreak, shortly after the RSV outbreak peak and probably related to it.<sup>18</sup> Moreover, it remains unclear whether the findings from elderly care home settings with relatively stable resident and staff populations can be extrapolated to acute care settings characterised by short lengths of stay and high patient throughput.

In the 2013/2014 and 2014/15 seasons, 55% of all frontline HCWs in England reportedly received the influenza vaccine<sup>19,19</sup>. Although the existing evidence is not strong and heavily weighted towards the benefits to residents of long-term care facilities, it is likely that vaccination of HCWs offers some indirect protection to high-risk patient groups. An increased focus should therefore be placed on vaccination of carers and HCWs in these settings.

Annual vaccination of individuals aged 65 years and over is also recommended in many national policies as a primary control measure. Initially, vaccine uptake amongst the elderly was low, but has substantially improved since the 1990s with achievement of the 75% target in England and the Netherlands by the 2008/9 season.<sup>20</sup> Concerns have been reported that the elderly are less able to mount an immune response following vaccination<sup>21</sup> with a paucity of studies to indicate effectiveness in this group.<sup>22</sup> While one RCT reported an efficacy of 58%<sup>23</sup>, the most recent Cochrane review<sup>24</sup> of 75 studies was unable to draw a conclusion about the effectiveness of vaccination (measured by onset of influenza like illness) based on pooled data from poor quality non-RCT studies. Vaccine effectiveness differs every season as it depends on the matching of vaccine and circulating strains.. Debate about the direct mortality reduction in the elderly<sup>25</sup> centres on potential different exposure risk in vaccinated and unvaccinated persons. Hence variation of the estimated effectiveness between places and seasons could obscure real protective effect on mortality, as evidenced by opposing interpretations of the Cochrane Review dataset.<sup>24, 26</sup> Despite the limited evidence, the influenza-associated hospitalizations and mortality in the elderly, may still justify vaccination, even if only moderately effective, to reduce this large burden of disease.<sup>27</sup>

Vaccination will not completely prevent transmission on its own, particularly in seasons with significant antigenic drift and mismatch between vaccine and circulating strains such as in the recent 2014-15 season.<sup>28</sup> While influenza immunisation is generally safe, immunity elicited by vaccination is shorter lived when compared to naturally acquired immunity, which may provide long-lasting

protection against subsequent infection. Modelling has suggested that repeated vaccination at a young age may increase the risk of influenza in older age, by a factor ranging between 1.2 to 2.4<sup>29</sup> but other research data contradicts this.<sup>30</sup>

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Given these limitations and the difficulties in achieving high annual vaccine uptake rates, the future may lie with the development of a universal vaccine that would not require seasonal administration.<sup>32</sup> Vaccination should only be seen as one element of a broad package of control measures including hand hygiene and use of appropriate barrier control measures.<sup>2,33</sup> While evidence exists for these, it remains poorly quantified.<sup>34,35</sup> Even when such control systems are in place, they may not always be adhered to. Compliance with hand hygiene for example has been reported to be as low as 40% in some health care settings.<sup>36</sup> Hygiene measures are often considered in isolation from vaccination and may attract more attention during outbreaks rather than primary prevention of infection. Within healthcare environments, viral shedding can be prolonged, possibly beginning at least one day before clinical illness with the duration depending on the age and immune status of the affected person.<sup>37</sup> Hand hygiene and administrative barrier control measures are therefore important in disrupting virus transmission.<sup>38</sup>

Control of transmission as it currently stands remains suboptimal and nosocomial influenza outbreaks continue to occur.<sup>39</sup> Further research is needed to fully understand the transmission of nosocomial influenza and the effectiveness of interventions to control spread. Epidemiological understanding

of transmission of influenza in the healthcare setting remains incomplete.<sup>37</sup> This is a complicated area of research due to multiple confounding factors. These include the source and route of viral transmission, clinical identification of cases (including serological classification which is challenging to interpret post vaccination), the patient's health status and effectiveness and implementation of any hygiene controls. Within studies ideally only specific endpoints for virologically confirmed influenza should be used, if possible reverse transcriptase polymerase chain reaction (RT-PCR), but often this is neither available nor feasible. Seasonal incidence of influenza is unpredictable and highly variable and thus assessment of interventions occurring during mild seasons with fewer than expected cases may be underpowered to assess specific outcomes.

In the absence of high quality evidence<sup>37</sup>, authorities advocate application of the 'precautionary principle' approach.<sup>40</sup> In practice this means applying a broad package of control measures in settings to most effect and further evaluating interventions as they are used. Efforts should be re-focused in order to have a greater overall impact on influenza transmission. Whilst emergent, but still quite limited, evidence confirms transmission between HCW and patients,<sup>37, 41</sup> other groups such as visitors and non-clinical staff are also likely to play a part, particularly in semi-closed settings such as elderly care homes. Such groups could be more closely engaged in preventative strategy and implementation. Higher risk 'health care' settings such as elderly care homes should also be clearly defined and targeted more closely with the full hierarchy of influenza control measures. This should be supported by consistent

messages from occupational health, public health and infection control professionals with wider public education.

Applying a traditional risk management approach such as the 'Hierarchy of Control'<sup>42</sup> may help to structure control measures in mitigating the risk of nosocomial infection in patients. As with any identified hazard, risk evaluation should lead to control measures which should start from the top of the hierarchy. Hence if the risk cannot be eliminated, the duty to control it to an acceptable level remains. Risk reduction may be achieved by limiting admission of patients to long-stay elderly care homes during outbreaks. This is particularly important when there is a laboratory confirmed RT-PCR influenza outbreak. Minimising visitors, especially children or any child/adult with symptoms during the seasonal flu period, immunising residents/patients, HCWs/care-staff and visitors and excluding any symptomatic staff who may still present for work are all important.<sup>43</sup> Hazard substitution is not possible. Engineering controls may include isolation where possible through single rooms, or distancing. Other measures include cough and sneeze etiquette, or personal protective equipment such as face masks for residents/patients and possibly carers (although limited evidence of effectiveness exists for this),<sup>44</sup> and especially hand washing.

Additional measures can be considered in acute care settings: isolating patients with suspected or confirmed influenza, limiting aerosol-generating procedures only to adequately ventilated single rooms before influenza can be excluded, provision of face masks for patients with acute respiratory infections until

symptoms abate,<sup>44</sup> checking and maintaining air-conditioning units and settings to avoid airflow imbalance, and providing HCWs with appropriate respirators, gloves, and gowns while performing aerosol-generating procedures. Finally, when an outbreak is detected in a nosocomial setting, currently NICE<sup>45</sup> and PHE<sup>46</sup> recommend consideration of neuraminidase inhibitors (NAIs) for post-exposure prophylaxis, alongside the physical and administrative infection control measures outlined above. The evidence for this is debated, with the latest Cochrane review concluding that using NAIs for prophylaxis “reduces the risk of developing symptomatic influenza”, although the authors also state that “the balance between benefits and harms should be considered.”<sup>47</sup> Administrative controls may include training and education of staff and visitors, and redeployment of unvaccinated staff where appropriate.

The current emphasis on HCW immunisation fosters the belief in health care providers that the duty of care to vulnerable patients and HCWs is discharged by merely implementing an employee influenza vaccination programme. However current controls are obviously suboptimal as outbreaks continue to occur. We need to reassess engagement and compliance with a broad set of control measures. Re-structuring and targeting efforts towards the higher risk settings, particularly elderly care homes, may have a greater overall impact. Risk assessments could determine where weaknesses in the hierarchy of control occur.

Influenza should be recognised and labelled as a ‘healthcare-associated infection’ (HCAI), given its associated morbidity/mortality and should have




similar focus and attention as the more commonly recognised HCAs such as MRSA.<sup>48</sup>

Whilst vaccination of HCWs is necessary, on its own it may not be sufficient to prevent nosocomial influenza infection and a multidimensional approach is clearly required. This is a much greater challenge than for occupational health alone and requires collaboration with public health, patient safety, infection control, quality and clinical governance functions. Commissioners of healthcare need a new multidisciplinary strategy (encompassing the full hierarchy of primary, secondary and tertiary controls) to reduce nosocomial influenza infections.

Word 1975

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