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Evidence Annex

Re: Correspondence 21st June 2018, Health care worker seasonal flu vaccination

Health care worker vaccination rates are high but very variable

England has one of the highest rates of influenza vaccination uptake in Europe across all target groups, including healthcare workers (HCW) (1). HCW vaccine uptake has increased from 10-15% in the early 2000s to 68.7% last year. There remain wide discrepancies across the country, the highest and lowest Trust uptake figures in 2017/18 were 92.3% and 38.9% respectively. There remains, therefore, significant scope for improvement.

Flu causes significant morbidity and mortality, with some groups at particular risk

In healthy adults, influenza is typically a mild self-limiting illness, and is therefore often not considered as a major cause for concern. However, influenza contributes to an average of 8000 deaths every year (2). Complications are more common amongst 'at risk' groups: people who are elderly, very young, pregnant, immunocompromised and those who have underlying chronic diseases (3). These groups are characterised by either pre-existing illness, which means that the complications of flu can be more severe, , and/or people in whom the vaccine response is itself poor.

Data from the 2010/2011 flu season below highlights the increased relative risk of flu related mortality amongst specific 'at-risk' groups (4).

	Number of fatal flu cases (%)	Mortality rate per 100,000 population	Age-adjusted relative risk*
In a risk group	213 (59.8)	4.0	11.3 (9.1-14.0)
Not in any risk group	143 (40.2)	0.4	Baseline
Chronic renal disease	19 (5.3)	4.8	18.5
Chronic heart disease	32 (9.0)	3.7	10.7 (7.3-15.7)
Chronic respiratory disease	59 (16.6)	2.4	7.4 (5.5-10.0)
Chronic liver disease	32 (9.0)	15.8	48.2 (32.8-70.6)
Diabetes	26 (7.3)	2.2	5.8 (3.8-8.9)
Immunosuppression	71 (19.9)	20.0	47.3 (35.5-63.1)
Chronic neurological disease (excluding stroke/transient ischaemic attack)	42 (11.8)	14.7	40.4 (28.7-56.8)
Total (including 22 cases with no information on clinical risk factors)	378	0.8	

Patients in healthcare facilities, especially where immunocompromised people are cared for, have a greater risk of harm

A higher proportion of patients in healthcare facilities and residents in long term care facilities (LTCF) are at risk of complications from influenza than the general population and the environment allows infection to spread quickly (14). One study from the USA comparing community onset and nosocomially acquired influenza found people with nosocomially acquired influenza were more likely to require admission to intensive care (42% vs. 17%) and had a longer length of stay (7.5 days vs. 3 days) (15).

It is known from a series of case reports that outbreaks in settings with immunocompromised patient groups are more prone to complications of influenza and experience higher mortality rates than the general population (5–13). Below is not a comprehensive list, but examples include:

- An post-pandemic outbreak of Influenza A(H1N1) in a haematology ward in Poland in which 9 out of 14 patients died (10).
- A case study from Japan during the 2009 pandemic found that of 7 patients with haematological cancers hospitalised with influenza, 3 required ventilation support and 3 patients died (11).
- An outbreak of influenza A in a teaching hospital in Guatemala found extremely high mortality rates in patients with AIDS (71%) (12).
- Two outbreaks occurring in transplant unit and oncology wards in a teaching hospital in Finland in 2014 found 8 out of 86 patients exposure to influenza A(H1N1) died. Patient vaccination had a significant protective effect (13).

The infectious period for influenza for most people begins one day prior to the onset of symptoms, peaks at 2-3 days after the onset of symptoms and subsides 5 days later (27). Infectivity is related to the period of viral shedding from the respiratory tract when the virus is spread through a combination of contact, droplets and aerosol transmission (28). Viral shedding can last much longer in immunosuppressed children and adults, those with chronic diseases and the elderly (5,29,30). This, along with the apparent high mortality from hospital outbreaks involving immunocompromised patients makes it especially important to reduce the risk of introducing influenza infection to areas of hospitals where immunocompromised patients are cared for.

Transmission of influenza in healthcare settings is an important risk for patients including those at greatest risk of complications

Spread of influenza is complex, with pathways which involve interactions between patients, staff, visitors and the environment. There are limitations in our understanding of influenza transmission in dynamic healthcare environments, reflecting the inherent challenges of conducting well powered randomised controlled trials and appropriately controlled observational studies.

It is however possible to study influenza outbreaks and identify individuals linked to the spread. One study addressed the risk of hospital-acquired influenza-like illness (ILI) in an acute care hospital over a 2 year period, with active surveillance and an attempt to link healthcare associated ILI cases to a source. The investigators found that patients exposed to an infected healthcare worker were 5.5 times more likely than other inpatients to develop influenza and patients exposed to other infected patients were 18 times more likely than other inpatients to develop influenza (16). Again this demonstrates the importance of reducing the risk of patients being in contact with either staff or other patients who are infected with influenza.

It is estimated that between 16-50% of people with influenza are asymptomatic (17–20). This will include people who are healthcare workers. Viral shedding in asymptomatic or mild cases of influenza is lower than in symptomatic cases but transmission is clearly possible when a person is unaware they are infected (21,22). One outbreak study suggested around 1 in 4 healthcare workers are infected with influenza every year which is likely to be higher than the general population (6).

Individual infectivity is highly variable and as a result transmission can derive from a small number of individuals. Of two studies conducted in laboratory conditions, one study found that 95% of infectious influenza particles derived from less than 20% of individuals (23), another found 98% of infectious influenza particles were from half the individuals (24). It is not possible to tell in advance who these individuals are.

Introduction of influenza to hospital settings is multifactorial. PHE outbreak investigations highlight the risks of unrecognised influenza cases admitted through emergency departments disseminating influenza through hospital wards. The lack of rapid and systematic testing of respiratory admissions for influenza and other viral infections contributes to this. There are clear indications that rapid point of care testing could improve implantation of appropriate infection control measures including isolation practices in hospitals (25) and has the potential to reduce downstream nosocomial infection (26)

Vaccination helps reduce transmission and is safe

Vaccinating adults under 65 years is significantly effective in reducing their risk of laboratory confirmed influenza infection. Vaccinating over 65s is still worthwhile but effectiveness against the vaccines used in recent years has reduced. It is therefore important to vaccinate healthcare workers, who will mostly be healthy under 65 year olds, to not only protect them, but by reducing their risk of infection help to reduce the risk to patients who are often elderly or vulnerable, for example because of immunosuppression.

Influenza vaccine effectiveness is typically around 30-70% in healthy adults <65 years which indicates a 30-70% reduction in the risk of developing laboratory-confirmed influenza. It is often lower in those over 65 years. In 2016/2017 there was no evidence of significant vaccine effectiveness against lab confirmed infection in primary care in the UK in this latter group (32) and this may again be the case in 2017/18. Despite high uptake, therefore, the direct benefits of vaccination in elderly patients is sometimes low (32). Vaccine

effectiveness is likely to be improved from 2018/19 by the introduction of adjuvanted trivalent vaccine for over 65s from 2018/19 and consistent use of quadrivalent vaccine in under 65s.

Side effects of influenza vaccination are typically mild, with some increase compared to placebo of short-lived fever 3% (vs. 1%), malaise 9% (vs. 6%), myalgia 18% (vs. 10%)(33) and local reaction at the site of injection. Allergic drug reactions are rare. There is no evidence of harms of vaccination beyond these side effects.

Research on HCW-patient transmission has mostly been undertaken in long term care facilities (LTCF). Three major systematic reviews are summarised below:

- A Cochrane review which was limited to randomised controlled trials (RCTs) found HCW vaccination had a small effect on lower respiratory tract infections, however, evidence was insufficient to draw definitive conclusion. The authors recommended large scale RCTs of residents to evaluate this issue (34).
- Two other systematic reviews included some observational studies:
    - One review found HCW vaccination was associated with a reduction in *all-cause mortality* in residents, however, had no impact on influenza-related mortality (35). This may reflect either difficulties of distinguishing influenza specific mortality or unadjusted confounders which were not considered in the study.
    - Another systematic review found HCW vaccination was associated with a general consistency in the protective impact of influenza vaccination in residents, albeit limited, however, the benefit could not be extrapolated to other individuals at risk of complications of influenza outside the LTCF setting (36).

Spread of influenza is a two-way relationship between healthcare workers and their household contacts. Vaccinating children is well recognised to have herd benefits on the wider community and should therefore be an effective way to reduce influenza in healthcare workers, who are mainly adults under 65 years, often with children in the household (37–39).

Evidence is inconsistent, but vaccination is likely to reduce staff absence

Systematic reviews have been inconclusive on the impact of influenza vaccination on time off work (40). Absenteeism may reflect several factors including the match of the vaccine (41) and culture of the workplace (42,43).

Recent observational evidence from an ecological study reported that a 10% increase in vaccination at trust level was associated with a 10% fall in sickness absence (44). This paper did not adjust for the childhood vaccination roll-out or the strain of flu circulating, and the end-point was all-cause illness absence which is non-specific. However, such observational evidence points to the need to seriously consider other confounders such as workplace culture which may explain the observed difference.

Hospital staff sickness policies vary, however, it is known that HCW with respiratory symptoms often continue to work (42,45,46). A recent study found that 40% of healthcare

workers reported working whilst affected by respiratory symptoms (42). There appears to be an over-reliance on fever as a diagnostic marker whilst this is known that a significant proportion of influenza cases do not present with fever (45).

Evidence therefore suggests a possible link between vaccination and reduced staff absence. It is, however, clear that health care workers infected with influenza are often not symptomatic or only mildly symptomatic, and even when symptomatic often remain in work. Together with vaccination, it remains critically important that staff who are unwell with respiratory symptoms exclude themselves from work but relying on policies to encourage symptomatic healthcare workers to stay away from work is inadequate to reduce risk of spread of flu to patients.

There are evidence based ways to improve vaccination levels

There is good evidence for a series of interventions which can increase uptake, such as making it easy for staff to take up the offer of vaccination, through a full participatory approach. This is as recommended in flu fighters information and likely to be reflected in guidance from NICE and PHE soon to be published. Over a quarter of trusts achieved staff vaccination uptake of 75% or above last year. There is considerable qualitative evidence in the literature on why HCWs choose to decline vaccination (47), however, locally gathered information may help individual trusts plan their flu strategy tailored to local circumstances.

Modelling studies suggest there is no threshold of herd immunity in HCWs and benefits continue to accrue in direct relationship to vaccination coverage (48). This highlights the benefits of exceeding the national target of 75% vaccination coverage amongst healthcare workers and aiming for continued improvement to maximum possible levels.

A recent systematic review of the qualitative evidence on HCW attitudes towards seasonal influenza vaccination identified a number of important and overlapping barriers to increasing vaccination rates, including: concerns about side effects, low vaccine effectiveness and perception that influenza is a minor illness which can be best controlled through hand hygiene and taking time off when ill. Interventions to increase the uptake of vaccination require balancing of individual autonomy of HCWs and the strength of the evidence on vaccination and the demonstrable harms and importance of other measures such as staff illness absence and infection control. Materials which are perceived not to be evidence based or approaches considered coercive are generally poorly received (48).

Whilst mandatory flu vaccination as a term of employment has the greatest impact on vaccination uptake, policies implemented in the USA, Canada and Finland have all been faced with substantial legal challenges. In Finland, the introduction of a mandatory programme in 2018 has resulted in a significant public backlash with a growing resistance to other vaccinations, including childhood programmes. This therefore needs to be balanced with other factors.

There is a clear professional duty for healthcare workers to be vaccinated in order to protect patients as part of a set of actions to control and prevent infection. Preventing avoidable illness and mortality amongst inpatients is central to the patient safety agenda and a clear responsibility of care providers, including frontline healthcare workers, to patients.

I understand the current plan for the NHS for winter 2018/19 is to work with Trusts to ensure that flu immunisation is ever more readily available for all staff. The intention is that being vaccinated becomes increasingly the norm, and that there should be a reduction in the significant variation that remains between Trusts. In addition, where healthcare workers actively decide not to accept vaccination you plan to gather information on a standard but anonymous form about the reasons for that refusal.

If you decide to add a more robust approach in specific clinical areas, my view is that there are two options:

1. That healthcare workers choosing not to receive vaccination should indicate the reasons on a form which is not anonymous. This is rational as professionals should be willing to own and justify decisions they make that have importance to the protection of patients in their care.
2. That these staff could be re-deployed to work in other clinical areas if that is compatible with maintaining the safe operation of service.

Which of these, or other strategies to use, is clearly a decision for NHS winter planning balancing the evidence with operational requirements.

When considered within a broader infection control and patient safety framework, engaging healthcare workers and improving transparency to build trust between HCWs, managers and administrators is likely to have greater benefits than actions which appear to be an external imposition (53). Weaknesses in the evidence should be acknowledged whilst taking action to target vaccination in healthcare workers.

Other interventions to reduce harm from influenza

Influenza viruses can survive on surfaces such as hands, glass or plastic for up to 24 hours, and on materials such as pyjamas, magazines and tissues for up to 2 hours, during which time the virus can spread (49). This is one potential means of transmission between staff and patients and between patients and other patients. It highlights the value of good hand hygiene and a clean environment (50).

There are a collection of viruses which present with similar symptoms to influenza and contribute to morbidity and mortality amongst vulnerable patients, however, influenza vaccine will provide no protection against these infections. Collectively these are known as 'influenza-like illness' (ILI) and include viruses such as rhinovirus, Human metapneumovirus and parainfluenza viruses. It is difficult to clinically distinguish influenza from other respiratory viruses without diagnostic point of care (POC) or laboratory testing. Reducing the spread of acute respiratory infections, including influenza, in hospital and social care settings requires a comprehensive package of every-day infection control measures, including hand-washing, respiratory hygiene, a clean environment and patient isolation (51,52). Point of care testing is clearly recommended to distinguish patients infected with influenza from their first attendance at hospital, so they can be appropriately cared for whilst reducing the risk of transmission to other patients and to staff in healthcare settings.

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Summary points

1. There is not perfect evidence but there are strong arguments to take a multi-pronged approach to reduce harm from influenza infection in healthcare settings. The importance of influenza as a contributor to unnecessary morbidity and mortality in vulnerable patients is consistently under-recognised.
2. Whilst rates of healthcare worker vaccination are high comparative to other countries there is still considerable variation and room for improvement, and there is no threshold above which extra benefits will not accrue.
3. Given the impact of influenza transmission in certain clinical settings, and the potential to reduce risk of transmission by staff vaccination, reducing the risk of transmission of flu in hospitals should be considered a patient safety issue rather than an optional additional step. As a result, both trusts and staff have a responsibility to ensure high rates of healthcare worker vaccination.
4. There is considerable evidence available to support actions to increase vaccination rates, including from Flu Fighters and forthcoming NICE and PHE guidance when published. These focus on making it easy for staff to be vaccinated and using approaches which specifically aim for full participation.
5. In considering clinical areas for further action to increase vaccination rates, reducing influenza in staff has potential to be most important where the patient group is at particularly high risk of complications of influenza, where the patient group is unlikely to respond well to vaccine themselves and where staff member provide intense individual care which involves close prolonged contact. These patient groups include vulnerable neonates and those who are immunocompromised with prolonged inpatient stays. Immunocompromised patients are especially vulnerable to morbidity and mortality from influenza infection. It is therefore rational to prioritise staff in those areas where these patient groups are concentrated, these being (in priority order):
    a. Clinical areas where the vast majority of patients are immunocompromised or vulnerable neonates – this would include Neonatal Intensive Care Units (NICU), oncology wards, and transplant units
    b. Other clinical areas where a high proportion of patients may be vulnerable, and receiving close one-to-one to clinical care. This would include adult and paediatric intensive care
6. In these areas the most straightforward additional step is for healthcare workers to state the reasons for not receiving vaccination on a non-anonymous form. In addition, the NHS could choose to redeploy, where compatible with maintaining service, to other clinical areas.
7. The range of actions required to reduce the harm from influenza infection in healthcare settings includes:
    a. Reducing the risk of flu in the general population by ensuring the wider vaccine programme remains successful and implementing the further planned roll out of the children's vaccine programme.
    b. Reducing the risk of healthcare workers becoming infected with influenza and therefore transmitting flu to patients and other staff, through achieving maximal

rates of healthcare worker vaccination with quadrivalent vaccine, and reducing their risk in the general community by ensuring implementation of the wider vaccination programme and especially the children's programme.

c. Reducing the risk of patients introducing flu infection into hospitals by increasing the availability of rapid diagnostics, including point of care testing as part of an overall approach, to enable the distinction between influenza infection and other causes of influenza-like illness and managing these accordingly.
d. Increasing the use of influenza antivirals early in the course of disease for people admitted with complications of influenza infection to minimise morbidity and mortality by increasing the availability of point of care testing at admission and raising the awareness of appropriate use of antivirals amongst front line clinicians.
e. Ensuring comprehensive infection control arrangements are in place at all times.

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