INTRODUCTION

The influenza virus continues to change and adapt, which may result in so called 'antigenic drift'. However, public health researchers' ability to characterise these changes is much enhanced. Influenza vaccination is the key public health intervention available to reduce the morbidity and mortality of influenza. Traditionally, the influenza vaccine has been trivalent (active against two different strains of influenza A and one strain of influenza B), but recently some influenza vaccines are available that are quadrivalent, containing two variants of influenza B. Practitioners have adopted a range of strategies to improve vaccine uptake, such as identifying eligible patients through their electronic health record and employing call-recall systems. Vaccination has occurred through a range of other settings: children of school age through their schools; adults at risk through pharmacies, and healthcare workers through their workplace.

Annual vaccination against influenza is well established in the UK. The traditional vaccination strategy has been to target groups at higher risk of severe disease following infection, such as adults and children with underlying chronic medical conditions; pregnant women; and older people. Although this approach has been shown to be highly cost-effective, a significant burden of disease remains because influenza continues to circulate in the population with a significant proportion of at-risk individuals remaining unprotected due to a lack of vaccination or limited response following vaccination. An alternative approach is universal vaccination offering vaccine to healthy children.¹

This strategy protects both the children themselves and, by reducing spread, indirectly protects those at higher risk of severe disease. This has led to the UK recommendation to offer a newly licensed live attenuated influenza virus (LAIV) vaccine to all children aged 2–16 years.² The programme started in 2013–2014 in children aged 2 and 3 years, and is being rolled out to older age cohorts over a number of seasons. Much of the influenza vaccine programme is delivered through primary care. Over recent years, there has been continuous improvement in the management of the administration of this vaccine. A recent new challenge has been the introduction of the childhood influenza vaccination programme offered to children aged 2–4 years through primary care.

Figure 1. Seasonal influenza vaccination coverage rates in older age groups in EU/EEA member states, 2011–2012 and 2012–2013 influenza seasons (n = 24 member states). © European Centre for Disease Prevention and Control, 2015.⁷

BENEFITS VERSUS RISKS OF INFLUENZA VACCINATION

The World Health Organization (WHO) clearly states that benefits of influenza vaccination vastly outweigh risks, a conclusion based on a series of evaluations of the effectiveness and safety of seasonal influenza vaccines.³ The cost-effectiveness of the selective strategy is well demonstrated. Though the risks are small, health authorities have developed monitoring strategies to ensure the seasonal influenza vaccine is safe, as even minor safety concerns can have a detrimental impact on uptake. Recently, the European Medicines Agency (EMA) released interim guidance for vaccine manufacturers to implement a system of enhanced surveillance to rapidly detect safety concerns before the peak of seasonal influenza immunisations.⁴ Initiatives like this are essential to ensure the safety of those eligible for vaccination, and to encourage uptake.

EFFECTIVENESS OF VACCINATING CHILDREN AND HEALTHCARE WORKERS

The vaccination of children with the newly licensed LAIV vaccine appears to have been effective in reducing the spread of influenza.⁵ The focus on vaccinating children against seasonal influenza stems from a rationale of immunising vectors of influenza, as this provides direct protection to the children themselves, but also has a larger effect on the spread of the disease in the population. Other groups who may readily spread influenza to vulnerable groups include healthcare workers, who are offered influenza

immunisation across the NHS; the vaccine uptake for this group up to January in the 2015–2016 season was around half (49%).⁶

VACCINE COVERAGE ACROSS EUROPE

The Netherlands and UK nations were the top five European Union members in terms of achievement of vaccine coverage for older age groups (>65 years in UK) during the 2011–2012 and 2012–2013 seasons (Figure 1).⁷ However, while Northern Ireland and Scotland reached the 75% uptake target for this group, England and Wales fell just short. There are a number of potential explanations for these differences across the UK, including the structure of the health service, delivery strategies employed, and attitudes to vaccination.

STRATEGIES TO INCREASE UPTAKE

A number of straightforward strategies are associated with improved vaccine uptake in primary care for patients aged >65 years and in a risk group: (a) having a lead staff member planning a campaign and producing a written report on coverage achieved an increase of 8% in uptake; (b) sending a personal invitation to patients resulted in a 7% increase; and (c) a lead member of staff running searches on the electronic health record to identify eligible patients improved uptake by 4%. For pregnant women, who remain one of the groups with the lowest uptake rates, having midwives carrying out vaccinations increased coverage by 4%.⁸

Pharmacist administration of the vaccine has been shown to improve uptake; even though it is not offered free at the point

of access, the convenience attracts patients across all age and social strata, especially healthcare workers.⁹ Administration of influenza vaccine at school is a well-established strategy to achieve high coverage among school-age children; the introduction of the LAIV programme in seven pilot areas in England (six of which implemented school vaccination) achieved a coverage of 52% and a consistent (though not statistically significant) reduction in cumulative disease incidence in the pilot sites relative to non-pilot sites.¹⁰

INFLUENZA VIRUS CHANGE

Influenza viruses are characterised through one or more tests, including genome sequencing (genetic analysis) and haemagglutination inhibition (HI) assays (antigenic analysis). These data are used to monitor changes in influenza viruses, and to compare the similarity of circulating strains with those included in seasonal influenza vaccines. The interpretation of genetic and antigenic data is complex due to a number of factors; for example, not all viruses can be cultivated in sufficient quantity for antigenic characterisation, so that viruses with sequence information may not be able to be antigenically characterised as well. During the winter of 2014–2015 there was antigenic drift (variation in the virus as a result of the accumulation of mutations within the genes that code for antibody-binding sites) in influenza A (H3N2) subtype viruses. The recommendation for that season's northern hemisphere H3N2 vaccine strain was an A/Texas/50/2012-like virus.¹¹ However, primary care influenza sentinel swabbing surveillance schemes in England found genetic and antigenic drift in circulating H3N2 viruses, with virus isolates antigenically distinguishable from the vaccine strain. The continued virological and epidemiological surveillance of influenza viruses is essential for provision of robust data aiding the selection of candidate influenza vaccine strains each year. Such changes are taken into account by WHO in its recommendations for subsequent seasons' vaccine formulations.

TRIVALENT OR QUADRIVALENT VACCINES

Most influenza vaccines administered in primary care for adults are trivalent (active against two different strains of influenza A and one strain of influenza B). However, some influenza vaccines are now quadrivalent and contain two variants of influenza B, particularly those for children. LAIV is a quadrivalent vaccine and appears to have few problems with reactogenicity;¹² as a live vaccine, it is also thought likely

to provide cross-protective immunity. Given the antigenic drift discussed above and the co-circulation of distinguishable strains every season, effective and safe vaccines against more strains can have a positive impact for the at-risk population.

CONCLUSION

Influenza infection can result in mortality and morbidity, especially in frail older populations and in residential settings, and influenza vaccination is a powerful mechanism for prevention. Although, generally, good vaccine coverage has been achieved across the UK, targets for specific groups have yet to be met in England and Wales. Practices should develop initiatives to encourage eligible patients to get vaccinated, as well as setting an example for other healthcare workers by ensuring that the practice staff receive the vaccine. Similarly, practices should not take it for granted that patients will present for vaccination, and should continue to promote vaccination against influenza for all who might benefit. The introduction of the new childhood influenza vaccination programme provides an exciting opportunity to further reduce the impact of influenza both in the targeted age groups, but also in the wider

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community. Vaccination against influenza remains as important as ever in primary care.

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REFERENCES

1. Baguelin M, Flasche S, Camacho A, *et al*. Assessing optimal target populations for influenza vaccination programmes: an evidence synthesis and modelling study. *PLoS Med* 2013; DOI: 10.1371/journal.pmed.1001527. Epub 2013 Oct 8.
2. Public Health England. *The flu vaccination winter 2015/2016. Who should have it and why*. 2015. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/451734/9407_PHE_General_Flu_A5_booklet_06b_web.pdf (accessed 9 Aug 2016).
3. World Health Organization. *Vaccines against influenza. WHO position paper*. 2012. http://www.who.int/immunization/position_papers/PP_influenza_november2012_summary.pdf (accessed 9 Aug 2016).
4. European Medicines Agency (EMA) Pharmacovigilance Risk Assessment Committee (PRAC). *Interim guidance on enhanced safety surveillance for seasonal influenza vaccines in the EU*. 2014. http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2014/04/WC500165492.pdf (accessed 9 Aug 2016).
5. Pebody RG, Green HK, Andrews N, *et al*. Uptake and impact of vaccinating school age children against influenza during a season with circulation of drifted influenza A and B strains, England, 2014/15. *Euro Surveill* 2015; DOI: 10.2807/1560-7917.ES.2015.20.39.30029.
6. Public Health England. *Seasonal influenza vaccine uptake amongst frontline healthcare workers (HCWs) in England. Winter season 2014 to 2015*. 2015. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/429606/Seasonal_Influenza_Vaccine_Uptake_HCWs_2014_15_Final_V2.pdf (accessed 9 Aug 2016).
7. European Centre for Disease Prevention and Control. *Seasonal influenza vaccination in Europe — Overview of vaccination recommendations and coverage rates in the EU Member States for the 2012–13 influenza season*. Stockholm: ECDC, 2015.
8. Dexter LJ, Teare MD, Dexter M, *et al*. Strategies to increase influenza vaccination rates: outcomes of a nationwide cross-sectional survey of UK general practice. *BMJ Open* 2012; **2**: e000851.
9. Anderson C, Thornley T. Who uses pharmacy for flu vaccinations? Population profiling through a UK pharmacy chain. *Int J Clin Pharm* 2016; **38**(2): 218–222.
10. Pebody RG, Green HK, Andrews N, *et al*. Uptake and impact of a new live attenuated influenza vaccine programme in England: early results of a pilot in primary school-age children, 2013/14 influenza season. *Euro Surveill* 2014; **19**(22): pii: 20823.
11. World Health Organization. Recommended composition of influenza virus vaccines for use in the 2014–2015 northern hemisphere influenza season. 2014. http://www.who.int/influenza/vaccines/virus/recommendations/2014_15_north/en/ (accessed 9 Aug 2016).
12. McNaughton R, Lynn E, Osborne V, *et al*. Safety of intranasal quadrivalent live attenuated influenza vaccine (QLAV) in children and adolescents: a pilot prospective cohort study in England. *Drug Saf* 2016; **39**(4): 323–333.