The World Health Organisation estimates that approximately one billion people are infected and up to 500 000 people die from influenza each year. The greatest burden of illness usually occurs among children, while the highest burden of severe disease (in terms of hospitalisation and death) occurs in those with underlying medical conditions, infants and young children, and elderly people. Current circulating influenza strains in humans include influenza A(H1N1)pdm09, influenza A(H3N2), and both influenza B viruses (B/Victoria and B/Yamagata). This article provides non-specialists with information on how to diagnose, manage, and prevent flu.

What is influenza virus?

There are four types of influenza viruses: influenza A, B, C, and D, but only influenza A and B viruses cause clinically important human disease and seasonal epidemics. Influenza A viruses cause the most severe clinical disease and are the commonest cause of seasonal epidemics and pandemics in human populations.

What are the symptoms of influenza?

Influenza is characterised by sudden onset of fever, myalgia, headache, malaise, dry cough, sore throat, and nasal congestion. The incubation period of influenza (time from infection to development of symptoms) is 1 to 4 days. Viral shedding, when the virus is infectious, usually occurs from one day before the onset of symptoms, to 5-7 days after. Influenza can cause severe illness or death, particularly in high risk populations.

How do influenza epidemics and pandemics occur?

Minor changes that occur in virus proteins between influenza seasons (known as antigenic drift) result in annual epidemics, with winter peaks in temperate regions (November-April in the northern hemisphere, and May-October in the southern hemisphere, see fig 2). In tropical and subtropical regions the seasonality of influenza is less well defined (fig 2). In contrast, pandemics (severe global epidemics) of influenza occur when a new influenza A subtype emerges abruptly because of a major shift in the proteins on the virus surface (antigenic shift), often because of combination with viruses circulating in animals. As most people have no immunity to the new subtype, infection spreads quickly (table 2).

How is influenza diagnosed?

Most influenza is diagnosed clinically in the community at times when the virus is known to be circulating. Patients admitted to hospital may have respiratory samples taken for testing by polymerase chain reaction (PCR), rapid antigen test, or immunofluorescence assay. With respiratory outbreaks in a closed setting (such as care homes, schools, hospitals) nasal swabs may be taken from the first few symptomatic individuals to identify the responsible organism.
What you need to know

- Influenza is an acute viral infection of the respiratory tract that spreads easily from person to person
- Influenza is usually self-limiting in healthy individuals, with recovery in 3-7 days
- Elderly people, children under 6 months old, pregnant women, and people with chronic conditions or immunosuppression are at increased risk of complications
- Offer antiviral treatment to people at risk of complications and increased influenza exposure, as well as to young children, who are efficient infection spreaders
- People in high risk groups may benefit from antiviral therapy, hospitalisation, or intensive care

**Box 1: Who should be prescribed antiviral treatment for influenza?**

Individuals at risk of influenza related complications

- Adults >65 years old
- Individuals with underlying chronic health conditions (chronic heart, lung, kidney, liver, neurological, and metabolic diseases, such as diabetes)
- Individuals with reduced immunity (such as after chemotherapy, asplenia, prolonged steroid treatment, splenic dysfunction, or HIV infection)
- Pregnant women, including up to two weeks post-partum
- Any other individual whom the clinician feels is at increased risk of developing complications from influenza
- Morbidly obese individuals (body mass index >40)

Individuals admitted to hospital with suspected or confirmed influenza

*Based on guidance from National Institute for Health and Care Excellence (NICE)*

**What treatments are available for influenza?**

Influenza is usually self limiting in healthy individuals. Treatment of uncomplicated disease in healthy individuals is supportive and includes antipyretics, adequate fluid intake, rest, and staying off work or school until 24 hours after resolution of fever to limit spread to others. Most randomised trials of antiviral drugs have been conducted among otherwise healthy individuals and have shown modest reductions in symptom duration (0.7 days). Fewer studies have been conducted among individuals at risk of complicated influenza. Data from observational studies and trials suggests that antiviral treatment may reduce adverse outcomes. For example, the meta-analysis from 2015 reported fewer lower respiratory tract complications requiring antibiotics after oseltamivir treatment compared with placebo (risk difference 3.8%) and fewer hospital admissions (risk difference 1.1%). NICE, Public Health England, UK Chief Medical Officers, and the WHO recommend treatment of suspected and confirmed influenza for individuals at risk of complicated influenza (box 1). General practitioners considering prescription of antivirals should discuss with patients likely benefits, as well as possible harms including nausea (number treated to cause nausea in one patient=28) and vomiting (number treated to cause vomiting in one patient=22).

Individuals with complicated influenza may be helped by antiviral treatment. Treatment is most effective if started within 48 hours of symptom onset, and it should not be delayed while awaiting results of investigations. Neuraminidase inhibitors oseltamivir and zanamivir inhibit viral release from infected cells and reduce the rate of viral replication. Meta-analysis of individual participant data found that, compared with late treatment, early treatment (within 48 hours of symptom onset) of hospitalised individuals with complicated influenza reduced the odds of mortality by 52%. Some individuals may require antibiotic therapy to treat secondary bacterial infections.

**How can influenza be prevented?**

**Vaccination**

Vaccination is the most effective means of preventing influenza and its complications. Immunity developed in one influenza season may not provide protection in future years mainly because of changes in circulating strains, antigenic drift, and waning immunity. Influenza vaccines are updated annually to include the viral strains that are predicted to circulate in winter. Box 2 lists the UK recommendations for vaccination. Vaccination schedules may vary internationally, and so it is important to check local policies. In healthy adults, trivalent inactivated vaccines have an overall vaccine efficacy of 60%, whereas newer quadrivalent vaccines are being increasingly adopted due to the broader protection provided by the inclusion of an additional influenza B virus.

Since 2013, the UK influenza vaccination programme has been extended to children aged 2-4 years, with planned phased introduction to children of school ages, as it reduces morbidity by directly protecting children and provides indirect protection to vulnerable groups (such as grandparents) by reducing transmission in the community. Attenuated live nasal spray formulation is recommended in children aged 2<17 years based on its superior efficacy and greater immunity against mismatched strains compared with inactivated vaccines. Studies have found that inactivated influenza vaccines cannot cause influenza disease and are safe in pregnancy.

Common side effects of vaccination include local injection site reactions and cold-like symptoms. Fever, malaise, and myalgia are less common. Contraindications include confirmed severe allergic reaction (anaphylaxis) to a previous influenza vaccine or to any component of the vaccine. Live attenuated influenza vaccine (LAIV) should not be given to children or adolescents with severe immunodeficiency or to those taking salicylate treatments because of the risk of Reye’s syndrome. LAIV is also not recommended for pregnant women or adults with immunosuppression.
Box 2: Who is offered influenza vaccination in the UK?25

**People at risk of influenza related complications***
- Adults over 65 years old
- Individuals with underlying chronic health conditions (for example, chronic heart, lung, kidney, liver, neurological, and metabolic diseases, such as diabetes)
- Individuals with reduced immunity (such as after chemotherapy, asplenia or splenic dysfunction, or HIV infection)
- Pregnant women
- Morbidly obese individuals (body mass index >40)

**People at risk of influenza exposure or transmitting influenza to vulnerable groups**
- Health and social care workers
- Individuals who live with or care for vulnerable people

**People living in settings where rapid spread is likely after introduction of infection, potentially resulting in high morbidity and mortality**
- Individuals living in long-stay care facilities

**Efficient influenza spreadsers**
- Children aged 2–<17 years

*Children <6 months old are not eligible to receive influenza vaccines and should be protected against influenza through vaccination of their mother during pregnancy.

Antiviral chemoprophylaxis

Influenza may be prevented or rendered less severe by post-exposure prophylaxis (PEP) with antivirals (oseltamivir and zanamivir).27, 29 NICE3 and Public Health England3 recommend that, when influenza is circulating, antivirals are offered to those who are:

- In at-risk groups (box 2) and
- Who have had close contact with people with confirmed or suspected influenza (that is, living in the same household or residential setting) and
- Able to start prophylaxis within 48 hours (oseltamivir) or 36 hours (zanamivir) of contact and
- Have not received vaccination in the current influenza season, or who have been vaccinated <14 days since contact or where there is significant mismatch between vaccine and circulating strains, or during an outbreak in a closed setting regardless of vaccination history.

Infection control and isolation

Although published evidence for effectiveness is limited, hand and cough hygiene are likely to be important interventions to reduce influenza spread in the community, as well as in closed settings (table 3).

During an outbreak, consider isolation of residents of closed settings for the duration of the infectious period (five days after symptom onset) to limit spread to others. Cohorting of patients (that is, in separate hospital bays or on separate floors of a residential home) may be necessary. Residential homes may need to be closed to new admissions until the outbreak is controlled. Care must be taken when discharging a patient from a ward with a known influenza outbreak to a care home, or vice versa.

New developments in prevention and treatment of influenza

Vaccine candidates have recently been developed that can elicit antibodies against multiple influenza strains, and thus could overcome the need for annual influenza vaccines. Several antiviral drugs are currently in development for influenza treatment, including favipiravir,29, 40, 41 nitazoxanide,29, 40 and arbidol.61, 62

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1 World Health Organization. Influenza (seasonal)—Fact sheet No 211. 2014. www.who.int/mediacentre/factsheets/fs211/en/
2 Cromer D, van Hoek AJ, Jit M, Edmunds WJ, Fleming D, Miller E. The burden of influenza in England by age and clinical risk group: a statistical analysis to inform vaccine policy. J Infect 2014;68:383-71. doi:10.1016/j.jinf.2013.11.013 pmid:24291062.
3 World Health Organization. Global Influenza Surveillance and Response System (GISRS). 2016. www.who.int/influenza/gisrs_laboratory/en/.
4 World Health Organization. Influenza vaccine viruses and reagents. 2016. www.who.int/influenza/vaccine/virus/en/.
5 Ferguson N, Edmund L, Epperson WB, et al. Characterization of a novel influenza virus in cattle and Swine: proposal for a new genus in the Orthomyxoviridae family. MBio 2015;6:e00003-14. doi:10.1128/mBio.00003-14 pmid:24995369.
6 Hause BM, Collin EA, Liu R, et al. A revision of the system of nomenclature for influenza viruses: a WHO memorandum. Bull World Health Organ 1989;56:503-9. pmid:2909132.
7 Webster RG, Bean WJ, Gorman OT, Chambers TM, Kawaoka Y. Evolution and ecology of influenza A viruses. Microbiol Rev 1992;56:152-79. pmid:1579108.
8 Lam PP, Coleman BL, Green K, et al. Predictors of influenza among older adults in the emergency department. BMC Infect Dis 2016;16:286. doi:10.1186/s12879-016-2027-9 pmid:2769517.
9 Olson DR, Heffernan RT, Paladini M, Konty K, Weiss D, Mostashari F. Monitoring the impact of influenza by age: emergency department fever and respiratory complaint surveillance in New York City. PLoS Med 2007;4:e247. doi:10.1371/journal.pmed.0040247 pmid:1763196.
10 Kumar S, Nant P, Ban E, et al. Influenza vaccination of schoolchildren and influenza outbreaks in a school. Clin Infect Dis 2011;53:130-6. doi:10.1093/cid/cir536 pmid:2160619.
11 Matsuzaki Y, Sugawara K, Furuse Y, et al. Genetic Lineage and Reassortment of Influenza C Viruses Circulating between 1947 and 2014. J Virol 2016;90:9251-65. doi:10.1128/JVI.00969-16 pmid:27384661.
12 Public Health England. PHE guidance on use of antiviral agents for the treatment and prophylaxis of seasonal influenza. Version 7.0, PHE, 2016.
13 Lam PP, Coleman BL, Green K, et al. Predictors of influenza among older adults in the emergency department. BMC Infect Dis 2016;16:286. doi:10.1186/s12879-016-2027-9 pmid:2769517.
14 Monte AS, Gravenstein S, Elliott M, Cotlove M, Schwarz M. Clinical signs and symptoms predicting influenza infection. Clin Infect Dis 2016;63:3243-7. doi:10.1093/cid/ci609688a.
15 Offen SE, Monte AS. Symptomatic predictors of influenza virus positivity in children during the influenza season. Clin Infect Dis 2006;43:564-8. doi:10.1086/503652 pmid:16868147.
16 Minodier L, Chardot RN, Cecchini PE, et al. Prevalence of gastrointestinal symptoms in patients with influenza, clinical significance, and pathophysiology of human influenza
Evaluation into practice

- What steps have you taken to improve the uptake of influenza vaccination among staff and eligible patients under your care?
- Have you reviewed your organisation’s infection control policy for responding to an outbreak of influenza-like illness?
- Have you reviewed antivirals prescribed (treatment or prophylaxis) for eligible patients with influenza and their close contacts?

Further educational resources

- Public Health England. Chapter 19: Influenza. In: Immunisation Against Infectious Disease. 2013, updated 2015. www.gov.uk/government/uploads/system/uploads/attachment_data/file/456568/2904394_Green_Book_Chapter_19_v10_0.pdf
- National Institute for Health and Care Excellence. Clinical Knowledge Summaries: Influenza-seasonal. https://cks.nice.org.uk/influenza-seasonal/
- Public Health England. Flu Plan: Winter 2016/17. www.gov.uk/government/uploads/system/uploads/attachment_data/file/525697/Annual_flu_plan_2016_to_2017.pdf
- Wellcome Trust & Academy of Medical Sciences. Use of neuraminidase inhibitors in influenza. 2015. www.acmedsci.ac.uk/policy/project-strategies/treating-influenza/
50 Siegel J, Rhinehart E, Jackson M, Centers for Disease Control and Prevention. Guideline for isolation precautions: preventing transmission of infectious agents in healthcare settings. CDC, 2007.

51 Health and Safety Executive. Pandemic flu—workplace guidance. HSE, 2016.

52 European Centre for Disease Prevention and Control (ECDC). Technical document. Safe use of personal protective equipment in the treatment of infectious diseases of high consequence: A tutorial for trainers in healthcare settings. Version 2, 2014.

53 Public Health England. PHE guidelines on the management of outbreaks of influenza-like illness in care homes. 2016. www.gov.uk/government/publications/acute-respiratory-disease-managing-outbreaks-in-care-homes.

54 Public Health England. Managing outbreaks of acute respiratory disease in care homes. 2012 (and supplement 2014). www.gov.uk/government/publications/acute-respiratory-disease-managing-outbreaks-in-care-homes.

55 Impagliazzo A, Milder F, Kuipers H, et al. A stable trimeric influenza hemagglutinin stem as a broadly protective immunogen. Science 2015;349:1301-6. doi:10.1126/science.aac7263 pmid:26303961.

56 Yassine HM, Boyington JC, McTamney PM, et al. Hemagglutinin-stem nanoparticles generate heterosubtypic influenza protection. Nat Med 2015;21:1065-70. doi:10.1038/nm.3927 pmid:26301691.

57 Joyce MG, Whealley AK, Thomas PV, et al. NISC Comparative Sequencing Program. Vaccine-induced antibodies that neutralize group 1 and group 2 influenza A viruses. Cell 2016;166:609-23. doi:10.1016/j.cell.2016.06.043 pmid:27453470.

58 Furuta Y, Gowen BB, Takashiki K, Shiroma K, Smaes DF, Barnard DL. Faviapravir (T-705), a novel viral RNA polymerase inhibitor. Antiviral Res 2013;100:446-54. doi:10.1016/j.antiviral.2013.09.015 pmid:24084488.

59 Rossignol JF, La Frazia S, Chiappa L, Ciucci A, Santoro MG. Thiazolides, a new class of anti-influenza molecules targeting viral hemagglutinin at the post-translational level. J Biol Chem 2009;284:29798-808. doi:10.1074/jbc.M109.029470 pmid:19638339.

60 Haffizulla J, Harman A, Hoppers M, et al. Nitazoxanide Influenza Clinical Study Group. Effect of nitazoxanide in adults and adolescents with acute uncomplicated influenza: a double-blind, randomised, placebo-controlled, phase 2b/3 trial. Lancet Infect Dis 2014;14:629-38. doi:10.1016/S1473-3099(14)70117-0 pmid:24852376.

61 Leneva IA, Russell RJ, Boriskin YS, Hay AJ. Characteristics of arbidol-resistant mutants of influenza virus: implications for the mechanism of anti-influenza action of arbidol. Antiviral Res 2009;81:332-40. doi:10.1016/j.antiviral.2008.10.009 pmid:19028526.

62 Pêcheur EI, Borisevich V, Halfmann P, et al. The synthetic antiviral drug arbidol inhibits globally prevalent pathogenic viruses. J Virol 2016;90:3586-92. doi:10.1128/JVI.02077-15 pmid:26739045.

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### Tables

#### Table 1 | Influenza viruses

| Influenza type | Classification | Reservoir | At risk groups |
|----------------|----------------|-----------|----------------|
| A              | • Classified into subtypes on the basis of haemagglutinin (H) and neuraminidase (N) antigens on the surface of the viral envelope.  
• To date, 18 haemagglutinin subtypes and 11 neuraminidase subtypes have been identified.  
• Only three haemagglutinin types (H1, H2, and H3) are recognised to cause epidemic disease in humans.  
• Nomenclature includes the virus type and subtype, natural host species, geographical origin, year of isolation, and strain number (such as H1N1A/duck/Alberta/35/76)² | The primary reservoir is aquatic birds, but viruses also circulate among many other species, such as pigs, horses, and sea mammals² | Infects people of all ages, but disproportionately causes severe disease in older adults and individuals with underlying chronic health problems |
| B              | Divided into lineages on the basis of the haemagglutinin glycoprotein | Mainly infects humans | Children are affected by influenza B infection at a disproportionately higher rate among the general population¹⁴ |
| C              | Unlike influenza A or B, which have two glycoproteins (HA and NA), influenza C has only one glycoprotein (HEF) | Mainly infects humans | Affects individuals of all ages, but tends to cause mild illness¹⁷ |
| D              | Little known about it, but is thought to be related to influenza C viruses | Mainly infects pigs and cattle | Not known to cause human disease¹⁵ |
**Table 2** Antigenic drift versus antigenic shift: implications for epidemics and pandemics

| Antigenic drift                                      | Antigenic shift                                      |
|------------------------------------------------------|------------------------------------------------------|
| Accumulation of mutations in genes that code for antibody binding sites on viruses | A sudden major change in the virus antigenicity leading to emergence of new strains |
| Only one virus strain (accumulation of point mutations) | From one or more virus strains (from genome reassortment) |
| Occurs frequently                                    | Occurs occasionally                                   |
| Usually responsible for seasonal influenza epidemics and affects effectiveness of influenza vaccine | Gives rise to pandemics, which occur irregularly and unpredictably due to a lack of immunity to the new strain in the human population |
| Occurs in influenza virus A, B, and C                | Only occurs in influenza virus A                       |
Table 3 | Responding to influenza cases and clusters or outbreaks by setting

| Interventions | Community setting | Care home setting | Acute clinical setting |
|---------------|-------------------|-------------------|-----------------------|
|               | At-risk patients | Low risk patients |                       |
| Isolation of patients | Avoid contact with other at-risk people and exclude from work, school, or childcare until asymptomatic | Avoid contact with at-risk people and exclude from work, school, or childcare until asymptomatic | Yes* | Yes |
| Use of PPE including surgical masks | Not recommended | Not recommended | Yes | Yes |
| Implementation of rigorous infection control procedures (hand hygiene; cough etiquette; environmental cleaning and waste disposal) | Provide advice on hand hygiene and correct cough etiquette | Provide advice on hand hygiene and correct cough etiquette | Yes | Yes |
| Symptomatic management | Yes | Yes | Yes | Yes |
| Antiviral therapy for patients with influenza | Recommended | Not recommended | Recommended† | Recommended† |
| Regular review to assess for clinical deterioration | Yes‡ | Not recommended | Yes‡ | Yes |

*If not possible or practical, consider cohorting of patients as soon as possible.
†Consider post-exposure prophylaxis for other at-risk patients and residents in hospitals and care home settings.
‡Have low threshold for referring to secondary care.
Figures

Fig 1 Symptoms and complications of influenza. Complicated influenza is defined as an infection that requires hospital admission.\(^{12}\)
Fig 2 Circulating influenza viruses reported to WHO through global laboratory surveillance systems for selected countries: 2015-16. Data from WHO FluNet Interactive https://pmacp.shinyapps.io/Influenza_isolates/