HEALTHCARE WORKERS HANDBOOK

ON

INFLUENZA

Last updated: May 2016

Compiled by the Centre for Respiratory Diseases and Meningitis,
The National Institute for Communicable Diseases (NICD)
a division of the National Health Laboratory Service (NHLS),

in collaboration with:

The South African National Department of Health

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division in the National Health Laboratory Service

DEPARTMENT OF HEALTH
Republic of South Africa

Review:
The first version of the Healthcare Workers Handbook on influenza, which was by drafted by the National Institute for Communicable Disease in collaboration with the National Department of Health (NDoH) was published in 2009. Annual updates have been published since 2010.

Summary of changes

Date Reviewed	Reviewed by	Summary of changes
April 2016	S Walaza	• Update on 2015 influenza season • Added information on effectiveness of influenza vaccine, including data from the 2015 South Africa influenza season • Updated information on influenza vaccine strains and vaccination recommendations for 2016 • Added information on types of influenza vaccines and vaccines available in South Africa • Updated information on the risk groups for severe influenza-associated disease, HIV-infected adults are listed as a separate group (these were included as part of underlying illness in previous versions). • Updated information on groups that are targeted for publically funded influenza vaccines.

Contents

Prefix and Disclaimer
This advice is based on currently available information regarding human infections caused by seasonal influenza viruses. Recommendations are based predominantly on current World Health Organization (WHO) and United States of America Centers for Diseases Control and Prevention (CDC) guidelines.

This material is intended for use by healthcare professionals. While the greatest care has been taken in the development of the document, the National Department of Health and the National Institute for Communicable Diseases of the National Health Laboratory Service do not accept responsibility for any errors or omissions. All healthcare professionals should exercise their own professional judgement in confirming and interpreting the recommendations presented in the handbook.

Acknowledgements
Expert specialists, including physicians, paediatricians neonatologists, infectious disease specialists and virologists, who provided valuable input in the drafting of these guidelines.

1 Background on influenza

1.1 What is influenza?

Influenza, commonly known as the "flu", is an acute viral infection of the respiratory tract caused by influenza viruses. There are three types of seasonal influenza viruses – A, B and C. Influenza A viruses are further categorized into subtypes. The 2009 pandemic influenza A(H1N1) virus (hereafter referred to as A(H1N1)pdm09) which appeared for the first time in 2009 causing a global influenza pandemic, is now a seasonal influenza virus that co-circulates with other seasonal viruses (namely influenza A(H3N2) and influenza B viruses. Influenza viruses are dynamic and evolve in unpredictable ways. Influenza viruses are further classified into strains based upon antigenic properties. Humoral immunity to influenza viruses is generally thought to be strain-specific and acquired through infection or vaccination. Seasonal influenza epidemics can be caused by new virus strains that are antigenically distinct from previously circulating virus strains to which a population has immunity; this is known as antigenic drift. Uncommonly, a completely new strain of influenza will emerge to which there is little or no existing immunity, this is known as antigenic shift and such novel strains can give rise to influenza pandemics.

1.2 Disease burden

Influenza viruses can cause disease in persons of any age, but overall rates of illness are highest in children. Usually, rates of severe illness and death are highest in persons aged ≥65 years; children aged ≤2 years, women who are pregnant or postpartum (within 2 weeks after delivery) and persons of any age with underlying medical conditions (risk factors) which increase the risk for influenza-related complications. During the influenza season in South African government facilities, approximately 14% of patients hospitalised with lower respiratory tract infection and 25% of patients with influenza-like illness will test positive for influenza on polymerase chain reaction (PCR). It is estimated that between 6 734 and 11 619 individuals die of seasonal influenza-associated illness in South Africa each year.[1, 2] Approximately 5% of these deaths are in children aged <5 years. Among individuals aged ≥5 years, an estimated 50% of influenza-associated deaths are in the elderly and approximately 30% are in HIV-infected individuals[2]. The highest rates of influenza-associated hospitalisation are in the elderly aged ≥65 years, HIV-infected individuals and children aged <5 years. [1-5]. Pregnant women also represent an important risk group for influenza-associated mortality. Among an estimated 646 - 1 428 seasonal influenza-associated deaths in women of childbearing age in South Africa in recent years, the majority (~90%) occurred in HIV-infected individuals and the influenza-associated mortality was three-fold higher (Relative risk 2.8, 95% confidence interval (CI)1 7 – 3.9) in pregnant compared with non-pregnant women[6]. Influenza infection may trigger exacerbations of diabetes and pulmonary (e.g. asthma) and cardiovascular disease. For this reason, people with underlying chronic medical conditions are at high risk of serious influenza complications, often resulting in hospitalisation and even death. Surveillance data from South Africa showed that having underlying illnesses (other than HIV) was a risk for influenza-associated mortality (odds ratio 2.9, 95% CI 1.2 - 7.3).[3]. Studies suggest that individuals with underlying tuberculosis may also be at increased risk of influenza-associated death [7, 8]. The burden of hospitalisations and deaths due to influenza can vary substantially from year to year depending on the transmission and virulence characteristics of the circulating strain.

1.3 Transmission

The virus is spread from person-to-person. It can be passed to other people by exposure to infected droplets expelled by coughing or sneezing that can be inhaled, or that can contaminate hands or surfaces. Influenza spreads rapidly especially in closed communities. The typical incubation period for influenza is 1-4 days (average 2 days). Most persons ill with influenza shed virus (i.e. may be infectious) from a few days before symptoms begin through 5-7 days after illness onset. However, very young children can be infectious for >10 days after illness onset; adults with severe disease (e.g. viral pneumonia) may also shed virus for >10 days, and severely immunocompromised persons can shed virus for even longer [9]. Children have the highest rates of seasonal influenza infection and illness in this group can amplify viral transmission in the community.

2 Clinical presentation and spectrum of illness

Infection due to influenza viruses can give rise to a wide range of clinical presentations, ranging from asymptomatic infection to severe illness and death. In the majority of people, influenza is an uncomplicated illness which is characterised by sudden onset of constitutional and respiratory symptoms such as fever, myalgia, cough, sore throat, rhinitis and headache. However, atypical presentations can occur. In some cases there may be gastrointestinal symptoms (nausea, vomiting and/or diarrhoea); these are more common in children than adults. Among young children, moderate complications such as otitis media have been reported commonly. Uncomplicated influenza illness resolves after 3-7 days although cough and malaise can persist for >2 weeks.

Influenza may be associated with more severe complications which include: viral pneumonia, secondary bacterial or viral infections (including pneumonia, sinusitis and otitis media), multi-organ failure, and exacerbations of underlying illnesses (e.g. pulmonary and cardiac illness). Rare complications include encephalopathy, myocarditis, transverse myelitis, pericarditis and Reye syndrome. For purposes of clinical management, influenza disease can be categorised as follows [10]:

- **Uncomplicated influenza:** ILI (Influenza-like Illness) presenting with fever, coryza, generalised symptoms (headache, malaise, myalgia, arthralgia) and sometimes gastrointestinal symptoms, but without any features of complicated influenza.
- **Complicated/severe influenza:** Influenza requiring hospital admission and/or with symptoms and signs of lower respiratory tract infection (hypoxaemia, dyspnoea, lung infiltrate), central nervous system involvement and/or a significant exacerbation of an underlying medical condition.

2.1 Risk factors for complicated/severe influenza

Certain groups of patients with influenza virus infection are at higher risk of developing severe or complicated disease. However, it should be borne in mind that influenza virus infection in any patient can result in severe/complicated illness. There are no early predictors of progression to severe disease. Persistent vomiting, high fever and progressive dyspnoea should alert the physician to this possibility. Patients may deteriorate rapidly.

Risk groups for severe/complicated influenza disease include:

- Infants and young children (particularly <2 years of age)
- Pregnant women (including the post-partum period)
- HIV–infected individuals
- Individuals with tuberculosis
- Persons of any age with chronic diseases, including:
    - Pulmonary diseases (e.g. asthma, COPD)
    - Immunosuppression (e.g. persons on immunosuppressive medication, malignancy)
    - Cardiac diseases (e.g. congestive cardiac failure), except for hypertension
    - Metabolic disorders (e.g. diabetes)
    - Renal disease
    - Hepatic disease

- Certain neurologic and neurodevelopmental conditions, including: disorders of the brain, spinal cord, peripheral nerve, and muscle such as cerebral palsy; epilepsy (seizure disorders); stroke; mental retardation; moderate to severe developmental delay; muscular dystrophy; or spinal cord injury.
- Haemoglobinopathies (e.g. sickle cell disease)

- Persons ≤18 years receiving chronic aspirin therapy
- Persons aged ≥65 years
- Persons who are morbidly obese (i.e. BMI ≥40).

2.2 Influenza in pregnancy

During the influenza season, pregnant women (at all stages including postpartum period, and especially those with co-morbidities) are at increased risk for severe or complicated influenza, particularly pneumonia, which may be rapidly progressive. Pregnancy related changes to the heart, lungs and immune system predispose the pregnant woman to more severe influenza disease, leading to increased risk of hospitalisation and severe outcomes including death. In addition influenza has implications for the outcome of pregnancy and may lead to spontaneous abortion, preterm birth or foetal distress. Infants are also at increased risk of developing influenza-associated complications. A randomised controlled trial from South Africa has demonstrated efficacy and safety of influenza vaccination in HIV-infected and HIV-uninfected pregnant women [11].

2.3 Influenza in children

Symptoms may be non-specific, therefore clinicians should maintain a high index of suspicion. Gastrointestinal symptoms (nausea, vomiting and/or diarrhoea) are more common in children than adults, and otitis media has been reported commonly with influenza illness in children. Influenza-associated encephalopathy (IAE) is an uncommon but serious complication with high mortality and neurological sequelae, occurring most often in children younger than 5 years. It has been increasingly recognised worldwide in association with influenza A (both H3N2 and H1N1) as well as influenza B virus infections. IAE is a rapidly progressive encephalopathy that usually presents within a few days of onset of typical influenza symptoms, and can manifest with diverse clinical symptoms including: seizures, altered/loss of consciousness, decreased cognitive processing including speech impairment, motor paralysis (mimicking Guillain-Barré syndrome) or sensory loss, abnormal or delirious behaviour, and focal neurological syndromes. CSF findings are usually normal, and neuroimaging may be normal or abnormal (diffuse abnormalities or focal white matter lesions). The diagnosis of IAE rests on confirmation of influenza virus infection in the absence of other causes of encephalopathy/encephalitis. Clinical management is generally supportive care. IAE may be accompanied by pneumonia.

3 Influenza season and recommendations for influenza vaccination for South Africa

3.1 Timing of the influenza season and vaccination

The South African influenza season falls in the winter months. The average onset of the influenza season over the past 31 years has been the first week of June. However, the season has started as early as mid-April and as late as the first week of July (Figure1 below, showing timing of the start, end and peak of the influenza season, South Africa 1984-2015).The average duration of the influenza season is 13 (7-25) weeks. Regular (monthly outside of the influenza season and weekly during the season) surveillance reports on current influenza activity in South Africa are available via the NICD website (www.nicd.ac.za). Influenza vaccines should be given sufficiently early to provide protection for the winter season. A protective antibody response generally takes about 2 weeks to develop following vaccination. Vaccination prior to the influenza season is ideal; however, it is never too late to vaccinate as the season lasts a few months.

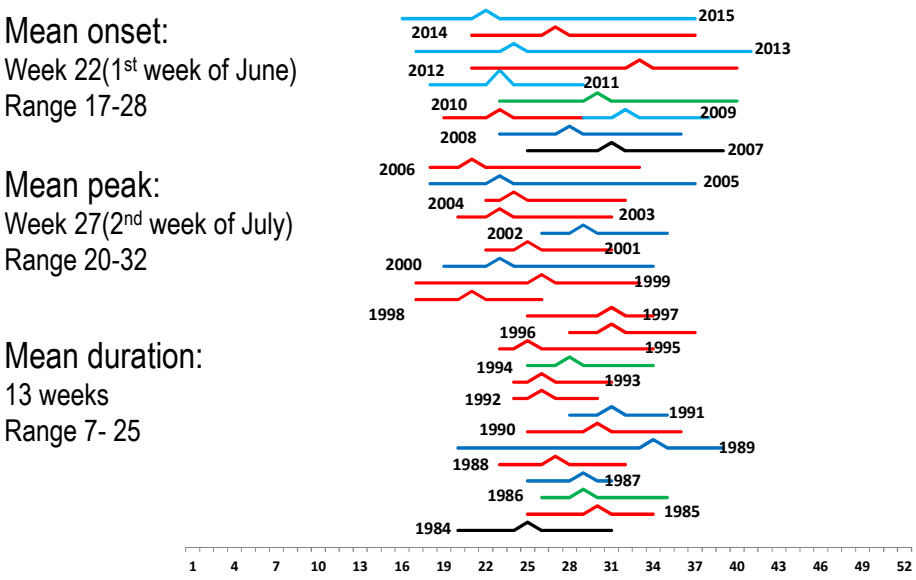

Figure1: Influenza seasons South Africa, 1984-2015

3.2 Circulating influenza types and influenza A virus subtypes in 2015

Seasonal influenza occurs annually, usually with co-circulation of influenza A and B viruses. The influenza season of 2015 was predominately influenza A (H1N1)pdm09 with additional co-circulation of influenza A(H3N2) and influenza B. Influenza B circulation increased towards the end of the season. The season started in week 16 (ending 19 April), peaked in week 23 (ending 7 June) and ended in week 37 (ending 13 September) (Figure 2). It is not possible to predict which type/s or subtype/s will predominate in the 2016 influenza season.

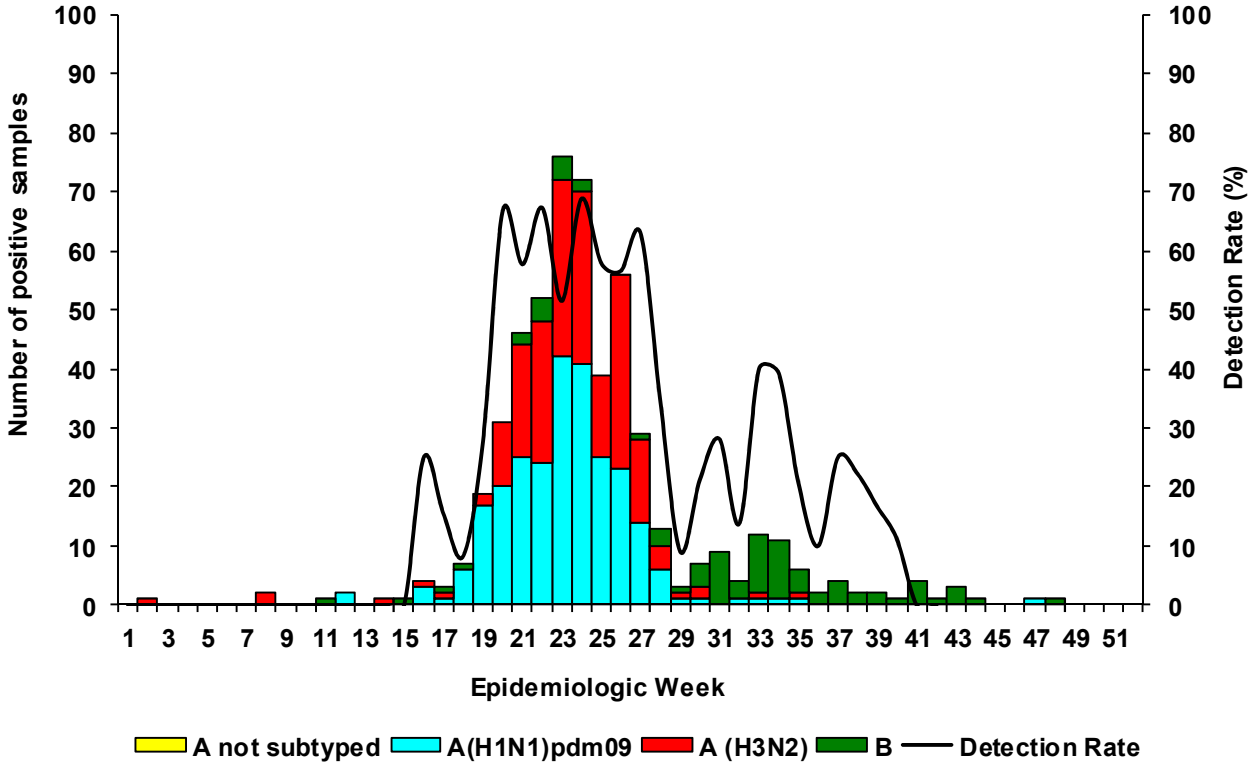

Figure 2 Number of positive samples by influenza types and subtypes and detection rate by week, viral watch influenza surveillance programme, South Africa, 2015

3.3 Influenza vaccination

Because of the changing nature of influenza viruses, WHO monitors the epidemiology of influenza viruses throughout the world. Each year recommendations about strains to be included in the vaccine for the following influenza season are made. Separate recommendations are made for the Southern Hemisphere and Northern Hemisphere vaccine strains each year.

3.3.1 Vaccine availability in 2015

The National department of health procured 922 800 doses of influenza vaccines for the 2015 influenza season and 89% (820390) of these were utilized. It is estimated that a similar number were distributed in the private sector in 2015.

3.3.2 Effectiveness of influenza vaccine

Influenza vaccine effectiveness depends on characteristics of those being vaccinated (age and health), whether there is a good match between the circulating viruses and the viruses contained in the vaccine, and on influenza types and subtypes. In general, influenza vaccines work best among children ≥ 2 years and healthy adults. Older people (≥65 years), children <2 years and severely immunocompromised individuals often have poorer immune responses to trivalent inactivated influenza vaccine (IIV) compared with healthy adults. However, even for these people influenza vaccine still provides some protection. Other products, e.g. high-dose influenza vaccine and adjuvanted vaccines, have been shown to be more effective in certain groups [12] but these vaccines are not available in SA. In the elderly, influenza vaccination has been shown to reduce the incidence of severe disease including bronchopneumonia, hospital admissions and mortality. Trivalent IIV has been shown to provide protection in HIV-infected adults without severe

immunosuppression [13]. Data are unclear as to the effectiveness in HIV-infected children aged <5 years [14].
Vaccination of healthcare workers may decrease the risk of spreading influenza to their patients.
Vaccinating individuals at risk of severe influenza may provide direct protection for these individuals. In addition, vaccinating individuals in close contact with people at risk for severe influenza may provide indirect protection through preventing transmission to high-risk individuals. Vaccinating children can protect children directly and the general population indirectly. This strategy is especially important for individuals in whom influenza vaccine is not indicated, such as children aged <6 months (who may be protected through maternal immunisation)[11, 15, 16]. A randomised controlled trial conducted in South Africa has shown that when pregnant women receive the influenza vaccine, their risk of developing influenza is halved, as is the risk to their infants in the first 24 weeks of life [11]. The vaccine has been shown not only to be efficacious for prevention of influenza in both mothers and their infants but also safe [11, 15, 16].
Recent influenza vaccination does not preclude a diagnosis of influenza as the vaccine is not 100% effective.

A meta-analysis including data from years when there was a mismatch between vaccine and circulating strains estimated a vaccine effectiveness (VE) of 59% (95% CI: 51-67) in healthy adults [17]. A systematic review and meta-analysis of published studies that used a test-negative design to assess influenza vaccine effectiveness reported variable pooled VE estimates between influenza types and subtypes, 33% (95% CI: 26-36), 54% (95% CI: 46-61) and 61% (95% CI: 57-65) for influenza A (H3N2), influenza B and influenza A(H1N1)pdm09, respectively.[18]. Previous studies from South Africa have shown influenza VE estimates of 54.2% (95% CI: 2 - 79), 57 % (95% CI: 15- 78), and 87% (95% CI: 67- 95), in 2010, 2011 and 2013 when there was a good match to the circulating strain and a VE of 38 % (95% CI: -72-78) in 2012 when the circulating A(H3N2) strain showed genetic drift [19]. During the 2015 influenza season, the estimated overall vaccine effectiveness, from the outpatient ILI, the Viral Watch surveillance programme, adjusted for age and underlying conditions, was 56 % (95% CI: 3- 81) against any influenza virus type; 60% (95% CI -8-85) against influenza A(H1N1)pdm09, 70% (95% CI: -28-93) against influenza A(H3N2) and 18% (95% CI -262- 82) against any lineage of influenza B. Despite low influenza vaccine coverage in South Africa in 2015, a moderate but statistically significant effectiveness was demonstrated (J. McAnerney, 2016).

3.3.3 Influenza vaccine strains and vaccination recommendations for 2016

Vaccination with the inactivated influenza vaccine (IIV) is recommended, where applicable. The formulation for the trivalent vaccine as recommended by WHO for the 2016 Southern Hemisphere influenza season is:

- an A/California/7/2009 (H1N1)pdm09-like virus
- an A/Hongkong/4801/2014 (H3N2)-like virus
- a B/Brisbane/60/2008-like virus

These recommendations include a change in the A (H3N2) and B strains when compared with the composition of the trivalent IIV used for the Southern Hemisphere during the 2015 season [20].
Standard-dose IIV should contain 15 µg of each haemagglutinin antigen in each 0.5 mL dose.

The IIV is available in both the public sector (at designated clinics and hospitals) and the private sector (at pharmacies, certain healthcare facilities, etc), generally from March or April each year.
"Recommendations pertaining to the use of viral vaccines: Influenza 2016" for South Africa have been published in the March 2016 edition of the South African Medical Journal[21]

3.3.4 Types of influenza vaccines and availability in South Africa*

Type	Trade name	Manufacturer	Presentation	Age indications	Route	Availability in SA
Trivalent IIV standard dose	Vaxigrip	Sanofi Pasteur	0.5ml liquid in a single- dose prefilled syringe	≥6 months	IM	Available
	Vaxigrip	Sanofi Pasteur	5.0ml multi-dose	≥ 6 months	IM	Not available

			vial			
	Fluvac	bioCSL	0.5 ml single dose prefilled syringe	≥9 years	IM	Available
			5.0 ml multidose vial	≥9 years	IM	
	Fluvirin	Novartis vaccines and diagnostics	0.5ml single – dose prefilled syringe	≥4 years	IM	
			5.0ml multidose vial	≥4 years	IM	
Inactivated influenza vaccine, cell based, standard dose	Flucelvac	Norvartis vaccines and Diagnostics	0.5ml single – dose prefilled syringe	≥18 years	IM	Not available
Trivalent IIV, High dose	Fluzone High Dose	Sanofi Pasteur	0.5ml single dose prefilled syringe	≥65 years	IM	Not available
Recombinant influenza vaccine, trivalent (RIV3)	Flu Blok	Protein Sciences	0.5ml single-dose vial	≥18 years	IM	Not available
Quadrivalent IIV standard dose	Fluzone	Sanofi Pasteur	0.25mls single dose prifilled syringe	6-35 months	IM	Not available
			0.5ml single – dose prefilled syringe/ 0.5 single dose vial	≥36 months	IM	Not available
			5.0 ml multidose vial	≥6 months	IM	Not available
	Fluarix	GlaxoSmithKline (GSK)	0.5ml single dose prefilled syringe	≥3 years	IM	Not available
	Flulaval	ID Biomedical Corp. of Quebec (distributed by GSK)	5.0 ml multidose vial	≥ 3 years	IM	
	Fluzone Intradermal	Sanofi Pasteur	0.1ml single dose prefilled microinjection system	18-64 years	ID	Not available
Live attenuated influenza vaccine	FluMist Quadrivalent	MedImmune	0.2ml single-dose prefilled intranasal sprayer	2-49 years	IN	Not available

*List may not be comprehensive other Trivalent inactivated influenza vaccine products may be available in South Africa, ID=intradermal, IN=intranasal, IM=intramuscular

3.3.5 Recommendations for use of vaccines

Persons to whom influenza vaccines should be administered:

1. Pregnant women irrespective of stage of pregnancy, or postpartum
2. HIV –infected adults
3. Healthcare workers
4. Persons (adults or children) who are at high risk for influenza and its complications because of underlying medical conditions and who are receiving regular medical care for conditions such as chronic pulmonary (including tuberculosis) and cardiac diseases, chronic renal diseases, diabetes mellitus and similar metabolic disorders, individuals who are immunosuppressed, and individuals who are morbidly obese (body mass index ≥40 kg/m^2)
5. Residents of old-age homes and chronic care and rehabilitation institutions
6. Persons aged ≥ 65 years
7. Children aged 6 months - 59 months (efficacy of trivalent IIV is low in this group)
8. Persons aged 6 months to ≤18 years on long-term aspirin therapy
9. Adults and children who are family contacts of individuals at high risk of severe influenza
10. Any persons wishing to minimise the risk of influenza acquisition, especially in industrial settings, where large-scale absenteeism could cause significant economic losses.

3.3.6 Target groups for the National Department of Health (NDoH) influenza vaccination campaign, 2016

Due to limited availability of the vaccine, not everyone can be vaccinated against influenza. The groups targeted by the NDoH for publically funded vaccines include:

1. Adults or children at high risk for influenza-related complications because of underlying medical conditions including: chronic pulmonary disease (including asthma), cardiovascular disease (except hypertension), renal, hepatic, neurologic, haematologic or metabolic disorders (including diabetes mellitus), morbid obesity (BMI ≥40), and immunosuppression (including HIV-infected persons)
2. Pregnant women – irrespective of stage of pregnancy
3. Children aged 6 months to 4 years (59 months)
4. Residents of old-age (nursing) homes and other chronic care or rehabilitation facilities
5. Children aged 6 months to 18 years on long-term aspirin therapy
6. All persons aged ≥ 65 years

(Please note that health care workers who fall into any of the above target groups should also be vaccinated)

3.3.7 Contraindications to influenza vaccination

The IIV is an inactivated vaccine, and has a well-established safety record. It is safe for use in pregnancy and in children ≥6 months of age. Contraindications to the administration of IIV include:

- A history of severe (anaphylactic) hypersensitivity to any components of the vaccine including, egg protein, or after previous dose of any influenza vaccine. Anaphylaxis is rare and a careful history will distinguish between anaphylactic reaction and allergic reactions like rashes. Mild egg protein allergy is not a contraindication for influenza vaccine.
- Infants <6 months of age.

3.3.8 Precautions to IIV administration include:

- Persons with moderate to severe illness with or without fever should preferably be immunised after symptoms have resolved
- Person who developed Guillian- Barrè syndrome within 6 weeks of receiving an influenza vaccine.

3.3.9 Influenza vaccine dosage and administration

The IIV should be administered intramuscularly (IM) as follows:

- Adults and children 6 years and above: Injection into the upper arm (Deltoid)
- Children aged 1 year to <6 years: Injection into the LEFT upper arm
- Infants aged 6 – 11 months: Injection into the LEFT antero-lateral thigh

NB: According to Department of Health recommendations, for children <6 years 13-valent pneumococcal conjugate vaccine (PCV-13) will be administered into the RIGHT arm.

The recommended dosage of influenza vaccine for patients of different age groups is described in table 1 [22].

Table1: Recommended dosage of influenza vaccine for patients of different age groups

Age Group	Dose	Number of doses
Adults and children 9 years of age and older	Adult dose (0,5ml) IMI	Single dose
Children 3 years through 8 years	Adult dose (0,5ml) IMI	1 or 2 doses†
Children 6 months through 2 years	0.25ml (half an adult dose) IMI	1 or 2 doses†

*Note: influenza vaccine is not recommended for infants <6 months of age.

†For individuals who have not previously received a total of ≥2 doses before March 2016, or when vaccine status is unknown, 2 doses should be administered ≥ 1 month apart.

3.4 Adverse effects of influenza vaccine

In trials, when IIV are administered, 16% - 20% of those vaccinated experience local reactions in the arm, lasting for one or two days. Short-term reactions (mild fever, malaise and muscle pains) have been reported in a much smaller proportion in the first few hours following vaccination. Trials of the split and subunit vaccines show even fewer systemic reactions. There have been no strong temporal associations/causal association of the current vaccines with more severe reactions. Anaphylaxis is very rare but does occur as with all vaccines. More severe adverse events, like Guillain-Barré syndrome have been reported with a particular vaccine in the 70s but they are extremely rare. With the modern influenza vaccines, the causative risk is either found to be very rare (0.8 per million doses) [23] or there is no causal link found at all [24-26] and more association is found with influenza infection than vaccination [27] .Influenza vaccination during pregnancy has been shown to protect both the mother and her baby (up to 6 months old) against influenza [15, 28-30]. Influenza vaccination is safe in pregnancy and influenza vaccines have been administered to millions of pregnant women over many years and have not been shown to cause harm to pregnant women or their babies [31].

4 Clinical management and considerations for treatment

Influenza causes approximately 7% of pneumonias in hospitalised children aged <5 years and 9% in individuals aged ≥5 years in South Africa [32, 33]. During the influenza season this increases to approximately 20%-40% of all people hospitalised for pneumonia. For this reason, influenza must be considered as an important potential cause of community acquired pneumonia (CAP) in all patients during the influenza season and consideration must be given to including oseltamivir as empiric treatment where indicated and available. Note that because influenza vaccination is not 100% effective in preventing influenza, a history of influenza vaccination does not exclude the possibility of influenza virus infection in patients with clinical features compatible with influenza.

Not all patients with influenza require treatment and initiation of treatment should be based on clinical judgment taking into consideration the patient's disease severity and progression, age, underlying medical conditions, likelihood of progressing to severe influenza, and time since onset of symptoms. When indicated, antiviral treatment should be started as early as possible, ideally within 48 hours, and should not be delayed by waiting for laboratory confirmation of influenza. However, antiviral treatment might still be beneficial in patients with severe, complicated or progressive illness, and in hospitalized patients when started after 48 hours of illness onset.

4.1 Who should receive influenza antiviral therapy?

Antiviral therapy is recommended as early as possible for any patient with confirmed or suspected influenza who

- has complicated or severe illness (including all hospitalised patients)
- is at higher risk for influenza complications (see section 2.0).

4.2 Antiviral therapy

Antiviral medications with activity against influenza viruses are an important adjunct to influenza vaccine in the control of influenza. Observational studies suggest that antiviral therapy reduces the risk of hospitalisation and death but this has not been confirmed in prospective, randomised clinical trials. Antiviral treatment is not indicated for treatment of influenza in persons who do not fall in the risk groups for severe influenza-associated disease who present with uncomplicated influenza. It is important to note that randomised controlled trials (RCTs) of antivirals in outpatients with mild disease do not inform clinical practice of patients with severe influenza or at increased risk of complications of influenza. There are no placebo controlled RCTs evaluating neuraminidase inhibitor treatment for hospitalised influenza patients. However, many observational studies of seasonal and pandemic influenza have found that neuraminidase inhibitor treatment of influenza in hospitalised patients is associated with reduced severe outcomes, including intensive care unit admission and death, especially when treatment is started within two days of illness onset**.** In the absence of appropriate RCT data on severe influenza, observational studies have important contributions to make to policy development. For this reason the South African guidelines continue to recommend the use of neuraminidase inhibitors for the treatment of hospitalised patients with confirmed or suspected influenza who have complicated or severe influenza or are at higher risk for influenza complications (see section 2.0).

4.2.1 Neuraminidase Inhibitors

Oral oseltamivir (Tamiflu®) and inhaled zanamivir (Relenza®) are chemically related antiviral medications known as neuraminidase inhibitors that have activity against both influenza A and B viruses. These two influenza antiviral medications are recommended for use during the 2016 influenza season.

4.2.2 Adamantanes

Amantadine and rimantadine are antiviral drugs in a class of medications known as adamantanes. These medications are active against influenza A viruses, but not influenza B viruses. These are not recommended for use due to high levels of resistance.

4.2.3 Antiviral resistance

Antiviral resistance to oseltamivir and zanamivir among circulating viruses is low, <1%. However antiviral resistance can emerge during or after treatment in certain patients (e.g. immunosuppressed). All the influenza positive strains from South Africa that were sequenced in 2015 were sensitive to oseltamivir. In contrast there is a high prevalence (>99%) of influenza A(H3N2) and influenza A(H1N1)pdm09 viruses resistant to adamantanes. Therefore, these are not recommended for antiviral treatment or chemoprophylaxis against currently circulating influenza A viruses. Continuous monitoring of the epidemiology, change in severity and resistance patterns of influenza strains may lead to change in guidance.

4.3 Antiviral medications recommended for treatment

The standard adult dose and duration of oseltamivir treatment is 75mg twice daily orally for 5 days. Doses for treatment are summarised in Table 2 [22]

Table 2: Recommended Dosage and Duration of Influenza Antiviral Medications for Treatment

Antiviral Agent	Children	Adults	Adverse events/allergic reactions
Oseltamivir (Tamiflu®)	**Neonates*** <38 weeks postmenstrual age : 1mg/kg twice a day 38- 40 weeks postmenstrual age:1.5 mg/kg twice a day	75 mg **twice** daily for 5 days	**Adverse events:** nausea, vomiting, Sporadic, transient neuropsychiatric events (self injury or delirium)
	Neonates and infants (1 day† -12 months) 3mg/kg twice a day		
	If ≥ 1 year, dose varies by child's weight ≤15 kg, the dose is 30 mg **twice** a day >15 to 23 kg, the dose is 45 mg **twice** a day > 23 to 40 kg, the dose is 60 mg **twice** a day >40 kg, the dose is 75 mg **twice** a day		
Zanamivir[4] (Relenza®)	10 mg (2X 5-mg inhalations) **twice** daily (**FDA approved and recommended for use in children 7 yrs or older**)	10 mg (2 5-mg inhalations) **twice** daily for 5 days	**Allergic reactions**: oropharyngeal or facial oedema. **Adverse events**: diarrhoea, nausea, sinusitis, nasal signs and symptoms, bronchitis, cough, headache, dizziness, and ear, nose and throat infection

Sources: Centre for Disease Control and Prevention. Antiviral agents for the treatment and chemoprophylaxis of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP).

*Current weight-based dosing recommendations are not appropriate for premature infants. Premature infants might have slower clearance of oral oseltamivir because of immature renal function, and doses recommended for full-term infants might lead to very high drug concentrations in this age group. Limited data from the National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group provide the basis for dosing preterm infants using their postmenstrual age (gestational age + chronological age). †US Food and Drug Administration approves >14 days old; however, experts agree should be used from 1 day[34].

4.3.1 Considerations for treatment with oral Oseltamivir

- Higher doses of oseltamivir are no longer recommended for critically ill patients as there is no clinical trial evidence confirming benefit [10, 35, 36]. Oral or enterically-administered oseltamivir has been reported to be adequately absorbed in critically ill adults, with standard doses producing therapeutic blood levels; and limited data suggests that higher dosing may not provide additional clinical benefit. Limited data suggest that oseltamivir administered orally or by oro/naso gastric tube is well absorbed in critically ill influenza patients, including those in the intensive care unit, on continuous renal replacement therapy, and/or on extracorporeal membrane oxygenation. Clinical judgement should guide decisions to prolong duration of treatment in patients with severe and prolonged illness.
- For patients unable to swallow capsules, methods for preparation of an oral suspension are described in instructions from manufacturers (refer to package insert). Where suitable suspending agents or diluents containing preservatives are not available, capsules can be opened and mixed with a measured volume of water (e.g. one teaspoon) immediately before administration. Such suspensions may be administered via nasogastric/orogastric tubes in mechanically ventilated patients.
- Renal impairment requires a dose adjustment for patients with creatinine clearance between 10 and 60 mL/min. and for patients with end-stage renal disease (ESRD) undergoing hemodialysis or continuous peritoneal dialysis receiving oseltamivir for the treatment or chemoprophylaxis of influenza. Oseltamivir is not recommended for

patients with ESRD not undergoing dialysis. Duration of treatment is the same as is the same as recommended for patients with normal renal function. (Table3)[22]

Table 3: Recommended doses of oseltamivir based on glomerular filtration rate

Glomerular filtration rate (ml/min)*	Recommended dose of oseltamivir treatment
61-90	75mg twice daily
31-60	30 mg twice daily
10 to 30	30 mg once daily
10	Seek specialist advice
Dialysis patients	Seek specialist advice

- Lower doses should be considered for infants who are not receiving regular oral feedings and/or those who have a concomitant medical condition which is expected to reduce renal function significantly.
- Capsule contents can be added to a sweet liquid / soft food immediately before administration to disguise bitter taste; syrup, condensed milk, yoghurt, sugar dissolved in water, or other sweet liquids/foods may be used. Open capsule/s and pour contents into a small amount of the liquid/food (one teaspoon maximum). Stir the mixture and ensure that the entire mixture is given to the patient. The mixture must be given immediately after its preparation.
- Methods for preparation of an oral suspension using capsules are described in instructions from manufacturers (refer to package insert). Where suitable suspending agents or diluents containing preservatives are not available, capsules can be opened and mixed with a measured volume of water (e.g. one teaspoon) immediately before administration.

4.3.2 Adverse Effects of Oseltamivir

- Nausea, vomiting, abdominal pain, diarrhoea, headache and conjunctivitis are the most commonly reported. Rash is uncommon. Other adverse effects that have been reported include: hepatitis, dysrhythmias, neuropsychiatric disorders (in children and adolescents), visual disturbances, Stevens-Johnson syndrome and toxic epidermal necrolysis.

4.4 Considerations for treatment with inhaled zanamivir

- Treatment with inhaled zanamivir is indicated in patients where oseltamivir-resistant influenza is demonstrated or highly suspected.
- Zanamivir is only recommended for use in persons aged ≥5 years.
- Zanamivir contains lactose (powder for inhalation) and must NOT be administered by a nebuliser. It may also interfere with ventilator functioning in ventilated patients.

4.4.1 Adverse Effects of Zanamivir

- Adverse effects are very rare and include: bronchospasm, respiratory impairment, angioedema, urticaria, and rash. Neuropsychiatric disorders have also been reported (especially in children and adolescents). Zanamivir is not recommended for people with chronic respiratory disease such as asthma or chronic obstructive pulmonary disease, which increase the risk of bronchospasm following administration.

4.5 Consideration for antiviral treatment for special groups and additional comments on management

4.5.1 Severely ill patients

- Antiviral therapy
    - Oseltamivir therapy should be started immediately upon admission. Treatment decisions should be based on clinical presentation and should NOT be delayed pending laboratory confirmation of influenza. Prolonged therapy may be of benefit but optimal doses and duration are uncertain. Decisions on whether to increase duration of treatment and / dose should be based on the clinical assessment and presentation, for example critically ill patients with respiratory failure or immunosupressed patients may have prolonged viral replication.

- Dose adjustment according to creatinine clearance is necessary for patients with renal impairment (Table 3).

- Other issues regarding critical care management of patients with influenza are beyond the scope of this document. A comprehensive review appears in the journal *Critical Care Medicine* 2010 Vol. 38, No. 4(Suppl.) pp e1-e142: H1N1 Novel Influenza: Pandemic Issues for Critical Care Practitioners. Free access is available online at: http://journals.lww.com/ccmjournal/toc/2010/04001

4.5.2 Pregnant patients

- Pregnant women (at all stages including postpartum, and especially those with co-morbidities) are at increased risk for severe or complicated influenza which may be rapidly progressive. Influenza in pregnancy carries an increased risk of adverse pregnancy outcomes, including spontaneous abortion, preterm birth and foetal distress. Consequently, pregnant women with suspected/confirmed influenza warrant close observation and early antiviral therapy. Treatment decisions should be based on clinical presentation and should NOT be delayed pending laboratory confirmation of influenza.
- Paracetamol is recommended for pain and fever. Salicylates and NSAIDs are contraindicated in pregnancy.
- There is currently no safety data on the use of higher doses of oseltamivir (>75 mg bd) in pregnancy.

4.5.3 Children

- Paracetamol is recommended for pain and fever. No salicylates should be given to children, since there is an increased risk of Reye syndrome with influenza and salicylates in younger children.
- Treatment of neonates and preterm infants should be done in consultation with a specialist in the field.
- Infants born to mothers with influenza DO NOT require antiviral therapy unless the infant has an influenza-compatible illness and requires hospitalisation.

4.5.4 Patients with persistent severe or progressive disease despite appropriate antiviral treatment

Patients who have laboratory-confirmed influenza where the clinical course remains severe or progressive despite ≥5 days of appropriate antiviral therapy (correct drug given at the correct dose etc.) should be investigated for the following:

- Bacterial secondary infections (particularly with *S. pneumoniae*, *S. aureus and S. pyogenes*) and nosocomial infections or underlying tuberculosis
- Presence of influenza-related complications (e.g. CNS involvement, myocarditis, rhabdomyolysis)
- Complications such as atelectasis or fluid overload
- Ongoing viral replication (as evidenced by laboratory tests): liaise with infectious diseases specialists/virologists regarding appropriate specialised testing. This may indicate infection with oseltamivir-resistant virus. Zanamivir is the treatment of choice for all patients where oseltamivir-resistance is demonstrated or highly suspected.

4.6 Chemoprophylaxis of influenza

Annual influenza vaccination is the best way to prevent influenza because vaccination can be given well before influenza virus exposures occur, and can provide safe and effective immunity throughout the influenza season. Antiviral chemoprophylaxis is currently NOT recommended. However, the WHO recommendations also advise that presumptive antiviral treatment may be of benefit in some higher risk situations, such as transplant patients, or patients with severe immunosuppression (e.g. those receiving chemotherapy) if any early signs of possible influenza infection are detected during the influenza season. Such higher risk individuals should be treated presumptively using a daily dose of the treatment regimen described above for duration of 7 days. Antiviral chemoprophylaxis for contacts of persons with influenza is currently not recommended. Guidelines issued by the Public Health England (PHE) for use in the United Kingdom, and by the Advisory Committee on Immunization Practices (ACIP) for use in the United States have made provision for the use of oseltamivir/zanamivir as chemoprophylaxis in certain outbreak settings and under certain conditions; however, these two sets of guidelines differ as to the intended target groups. Common to both sets of guidelines is the major proviso that chemoprophylaxis must be given within 48 hours of last contact with a person ill with influenza in order to be effective, in addition to other control interventions.

Although CDC does not recommend widespread or routine use of antiviral medications for chemoprophylaxis they do recommend antiviral chemoprophylaxis to control outbreaks among high risk persons in institutional settings and in addition advise that prophylaxis can be considered in the following situations [22]:

- Prevention of influenza in persons at high risk of influenza complications during the first two weeks following vaccination after exposure to an infectious person
- Prevention for people with severe immune deficiencies or others who might not respond to influenza vaccination, such as persons receiving immunosuppressive medications, after exposure to an infectious person
- Prevention for people at high risk for complications from influenza who cannot receive influenza vaccine due to a contraindication after exposure to an infectious person
- Prevention of influenza among residents of institutions, such as long-term care facilities, during influenza outbreaks in the institution.

The PHE recommends targeted use of antivirals as post exposure chemoprophylaxis for patients at high risk of complicated influenza and severely immunocompromised patients [10].

It is therefore advised to follow the WHO guidelines in this regard, and to seek specialist advice when indicated.

4.7 Other interventions for management

- **Oxygen therapy:** Monitor Oxygen saturation and maintain SaO_2 >90% (92-95% for pregnant women) with nasal cannula or face mask. High flow oxygen may be required in severe cases.
- **Antibiotics:** In cases of pneumonia, early empiric treatment for community-acquired pneumonia is advised. Since there is an increased risk of secondary infection with *S. pneumoniae*, *S. aureus and S.pyogenes*, co-amoxiclav is a suitable empiric antibiotic. Submit appropriate specimens for microscopy culture &sensitivity (MC&S) to laboratory, and tailor antibiotic/s accordingly. Exclude a diagnosis of tuberculosis.
- **Corticosteroids:** Low doses of systemic corticosteroids may be considered for patients in septic shock who require vasopressors, or when indicated for another reason (adrenal insufficiency, COPD, asthma exacerbation). However, systemic corticosteroids are NOT recommended as adjunctive treatment for severe influenza. A Cochrane review that included observational studies published between 1974 and 2015 found that adjunctive corticosteroids was associated with increased mortality. On meta analysis, corticosteroid therapy was associated with increased mortality OR 3.1 (95% CI 1.6-5.9)[37].
- **Paracetamol / acetaminophen:** Administer for fever or relief of fever-related symptoms.
- There are insufficient data on efficacy, safety or both for the following agents and their use is therefore not recommended at present: immunoglobulins, intranasal interferons, arbidol, ribavirin, and favipiravir.

5 Laboratory testing

5.1 Who should be tested?

Laboratory testing of uncomplicated illness (patients who fit the ILI case definition) is **NOT** routinely recommended, as it provides very little advantage to the clinical management of individual patients. Testing is recommended for the following patients:

- Patients who meet the criteria for complicated or severe influenza, where a laboratory diagnosis will assist in patient management, or patients hospitalised due to a lower respiratory tract infection where no other explanation for illness is evident and influenza forms part of the differential diagnosis.
- Patients at risk for developing complicated or severe influenza (as per list under section 2.1) AND who are symptomatic should be considered for testing if it will guide clinical management.
- Clusters of cases where a diagnosis of the cause of the outbreak is needed (e.g. within institutions such as healthcare facilities, nursing homes). First 2-3 cases to be tested, thereafter testing not required.
- An individual who has died where influenza is suspected as the cause of death.

Important note: **Initial treatment decisions should be based on clinical presentation and should NOT be delayed pending laboratory confirmation of influenza.**

Note: These recommendations for laboratory testing do not apply to surveillance activities managed by the NICD (e.g. Viral-Watch, pneumonia surveillance programme), and testing should continue as guided by those individual surveillance programmes.

5.2 Laboratories conducting testing

The NICD is no longer offering routine diagnostic tests, including for influenza outside of the established surveillance programmes at specific sites. Diagnostic capacity to test for influenza virus and/or serotyping has now been established in various public- and private-sector laboratories throughout the country.

Clinicians are urged to discuss with their facility's designated laboratory about:

- where specimens should be referred,
- the specific test that will be conducted by that laboratory and the interpretation ± limitations thereof, and
- the cost implications to the hospital/patient/medical aid.

5.3 Influenza Tests

In line with WHO recommendations, molecular diagnostics are currently the method of choice for influenza virus detection. While the specificity is high, the sensitivity of currently available rapid-point-of-care or immunofluorescence tests designed for direct detection of influenza A viruses is low and therefore not recommended at present. False negative results occur commonly with rapid influenza diagnostic tests (RIDT) that detect influenza viral antigens. A negative RIDT result does **NOT** exclude a diagnosis of influenza in a patient with suspected influenza and should not preclude starting empiric antiviral treatment.

5.4 Specimen collection, storage and transportation

i. Healthcare workers performing respiratory sample collection should practice appropriate infection prevention and control measures (see section 6.1 below). Wear appropriate personal protective equipment, including a medical mask and non-sterile gloves; wear eye-visors or goggles or a face shield if procedures include a risk of splash to the face. When performing specimen-collection procedures that may generate aerosols (e.g. aspiration or open suctioning of the respiratory tract), a particulate respirator (e.g. fit-tested N95 respirator) must be worn, in addition to gloves, eye-visors/goggles or a face shield.
ii. Combined nasopharyngeal and oropharyngeal swabs in viral/universal transport medium (VTM/UTM) are the preferred specimen. Swabs pose a lower risk of transmitting infection to healthcare workers than do nasopharyngeal aspirates (NPA) or nasal washes, both of which may generate aerosols. Swab each nostril with a single swab,(swab to reach depth equal to distance from nostril to outer opening of ear). Leave swab in place for a few seconds to absorb secretions. Slowly remove swab while rotating it. Use a second swab to swab the throat. Use flocked swabs or dacron or rayon swabs if flocked swabs are not available (wooden shaft swabs are not suitable for testing). Place both swabs into the same container of UTM. Snap off the tip at the marked break point.
iii. If using the Virocult ® specimen collection and transport device, remove the swab from its holder and swab the nostrils/throat. Place the swab into the transport tube, secure the cap, and squeeze the end of the tube around the sponge to ensure complete wetting of the swab tip.
iv. Complete the specimen request form with the following details: patient name, health facility (where appropriate), healthcare worker's name and contact numbers, lab name, contact person, telephone and fax number for receipt of results, and clinical details.
v. Transport specimens directly to the appropriate laboratory (see section 5.2). The specimens must be transported at 4^0C if transport is expected to be delayed.

The following additional information should also be taken into account regarding specimen collection:

- Specimens for virus isolation or for detection of viral nucleic acids or antigens should be taken preferably during the first three days after onset of clinical symptoms, but may be taken up to a week after onset or even later in severely ill or immunocompromised patients or children.

- Specimens should preferably be taken prior to commencement of antiviral agents but can still be taken a few days after initiation of antiviral treatment, especially in patients who are getting worse on antiviral treatment. In these cases antiviral resistant virus infection should be considered and testing for Oseltamivir resistant virus infection may be considered.
- In addition to swabs from the upper respiratory tract, invasive procedures such as bronchoalveolar lavage/ bronchial aspirate or lung biopsy can be performed for the diagnosis of influenza virus infection of the lower respiratory tract where clinically indicated. For example, ventilated patients who do not have a confirmed diagnosis of influenza but in whom influenza is suspected, should have lower respiratory tract specimens collected for testing as these patients may have already cleared the influenza virus from the upper respiratory tract.
- Results of all diagnostic tests for influenza are dependent upon several factors (including specimen type and quality of specimen collection, timing of collection, storage and transport conditions), such that false-negative results may be obtained. When clinical suspicion is high, clinicians must consider repeat/serial testing. Lower respiratory tract specimens may yield the diagnosis when testing of upper respiratory tract specimens is negative. Multiple respiratory tract specimens collected on different days should be tested if influenza virus infection is suspected but a definitive diagnosis has not been made.

5.4.1 Post-mortem specimens

A variety of specimens can be collected post-mortem; all specimens (swabs/tissue) need to be placed directly into viral transport medium. Suitable specimens include:

- Nasal, nasopharyngeal and throat swabs
- If consent has been given for a post-mortem, tissues that may be sampled include lung, trachea (proximal and distal), nasopharynx (best done from a supratentorial approach with removal en bloc), liver, brain and kidneys
- If consent for a full post-mortem is not forthcoming, the attending clinician should consider a para-mortem Trucut lung biopsy (following obtaining consent from next-of-kin). Other organs which may be sampled using a Trucut biopsy needle include spleen, bone marrow and liver.

5.5 Materials for specimen collection

1. Wooden shaft swabs are not suitable for respiratory virus PCR. Please use flocked, dacron or rayon swabs.
2. All specimens must be transported in UTM as instructed above.
3. The appropriate swabs and UTM may be obtained from your local laboratory.
4. Laboratories should stock UTM and the appropriate swabs, which may be obtained through their usual suppliers.

6 Infection prevention and control (IPC)

Human-to-human transmission of influenza viruses occurs either directly or indirectly through close, unprotected contact with large respiratory droplets. The role of smaller droplet nuclei at close-range exposure in transmission of influenza is not known, but may be more important in certain settings (e.g. aerosol-generating procedures associated with increased risk of virus transmission). Therefore, IPC precautions need to be focused on controlling respiratory droplet spread.

6.1 IPC precautions

Recommended IPC precautions when caring for patients with suspected, probable, or confirmed infection with influenza viruses, or ILI include the following:

- When working in direct contact with patients, Standard and Droplet Precautions should be applied:
    - Standard Precautions:
        - Hand hygiene: washing hands with soap and water or the use of an alcohol-based hand rub
        - Use of personal protective equipment (PPE): this includes facial protection (by means of a medical mask and eye-visor /goggles or a face shield) as well as use of a gown and clean gloves.
    - Droplet Precautions:
        - Wear a medical mask if working within approximately 1 metre of the patient or upon entering the room/cubicle of a patient on Droplet Precautions
        - Perform hand hygiene before and after patient contact and immediately on removal of a medical mask

- IPC precautions when performing aerosol-generating procedures associated with an increased risk of infection transmission (e.g. aspiration/open suctioning of the respiratory tract, including for the collection of respiratory tract specimens, intubation, resuscitation, bronchoscopy, autopsy):
    - Wear a particulate respirator (e.g. fit-tested N95 respirator), a clean non-sterile long-sleeved gown, and gloves.
    - Perform hand hygiene before and after patient contact and after PPE removal
- IPC precautions for patients who are mechanically ventilated or undergoing respiratory therapy:
    - Mechanically ventilated patients: Standard and Droplet Precautions (but when aerosol-generating procedures are performed, particulate respirators need to be worn).
    - Chest physiotherapy: Standard and Droplet Precautions. A medical mask should be worn by the patient if possible.
    - Nebulisation: Standard and Droplet Precautions.

6.2 Duration of isolation precautions

- All patients should remain on droplet precautions for a minimum of 7 days following symptom onset.
- Droplet precautions should be maintained until 24 hours following resolution of fever. However, standard precautions remain in effect for all patient care. Certain groups of patients may have prolonged viral shedding which extends beyond resolution of acute symptoms, such that there may still be a risk of influenza transmission in the absence of symptoms. These include:
    - Infants and children
    - Elderly patients
    - Severely immunosuppressed or immunocompromised patients: these individuals may shed more virus for a longer time period and are at increased risk for development of antiviral-resistant virus. For such patients, Droplet Precautions should be maintained for the duration of the illness.

6.3 Respiratory hygiene/cough etiquette

All persons (healthcare workers, patients, and visitors) should cover their mouth and nose with a disposable tissue when coughing or sneezing, then discard the tissue in a receptacle and perform hand hygiene (washing hands with soap and water or the use of an alcohol–based hand rub). Alternatively, if they do not have a tissue, they can cough/sneeze into their upper arm. When possible, patients who are showing signs of an ILI should wear a medical mask in waiting areas etc. Individuals who are not well should be encouraged to stay home and keep some distance from healthy people, as much as possible.

6.4 Health Care Providers and Occupational Health

Annual influenza vaccine is recommended for healthcare providers to protect not only themselves against influenza, but perhaps more importantly their patients and vulnerable colleagues. Healthcare providers are especially at risk of occupational exposure to influenza and if infected can pass the infection on to their patients, particular those at high risk of complications of influenza such as infants, pregnant women and immune-compromised patients. Infected healthcare providers can pass on influenza viruses even if they do not feel ill. Vaccinated HCW would be protected themselves and act as a barrier against the spread of influenza in healthcare facilities as well as maintain healthcare delivery during outbreaks. Healthcare workers absent because of influenza place extra burden on colleagues.[38]. However, low rates of vaccine uptake have been reported among healthcare providers. HCWs with symptoms should stay at home. Because of their close proximity to patients, HCW can pass on the influenza virus to their patients. However, several studies have shown that more than 75% of healthcare providers continue to work despite being infected with influenza [39]. While Influenza vaccine effectiveness varies from year to year taking the vaccine in autumn does decrease the risks of influenza especially in those vulnerable to complications. HCWs at high risk for severe disease and complications of influenza should follow recommended IPC measures carefully.

Health professionals have been identified as the most important source of information on vaccination for the general public. They are key players in communicating information and encouraging the final decision to be vaccinated. The willingness of health professionals to recommend immunization is crucial [40]. Data from a Knowledge, attitudes and practises (KAP) survey conducted among VW practitioners (VWP) in South Africa, showed that VWP, who are mostly private practitioners,

had good knowledge of the benefits of influenza vaccine, 82/96 (85.4%) agreed that vaccinating health care workers protected patients from becoming infected with influenza and 87/96 (90.6%) had previously been vaccinated against influenza and had received the vaccine in 2012. However, despite this knowledge, influenza coverage remains very low among their patients [19]. In order to achieve high coverage, the annual influenza immunization coverage in health care providers in every health facility should be reported, and misconceptions (knowledge and attitudes about influenza and the vaccine) and organizational challenges (availability and access) addressed. Influenza vaccine should be integral to infection control, barriers to coverage addressed, plans to effectively improve coverage developed and implemented, and quality standards linked to an increase in budget allocation for health facilities maintaining high influenza vaccine coverage in Health Care Providers.[41, 42].

6.5 Resources for further information

WHO guidelines:

- WHO guidelines for pharmacological management of pandemic influenza A(H1N1) 2009 and other influenza viruses (revised February 2010): http://www.who.int/csr/resources/publications/swineflu/h1n1_guidelines_pharmaceutical_mngt.pdf
- Recommended composition of influenza virus vaccines for use in the 2016 southern hemisphere influenza season : http://samj.org.za/index.php/samj/article/view/10586
- Clinical management of human infection with pandemic (H1N1) 2009: revised guidelines (November 2009): http://www.who.int/csr/resources/publications/swineflu/clinical_management_h1n1.pdf
- Infection prevention and control during health care for confirmed, probable or suspected cases of pandemic (H1N1) virus infection and influenza-like illness (Updated guidance, 16 December 2009): http://www.who.int/csr/resources/publications/cp150_2009_1612_ipc_interim_guidance_h1n1.pdf

Centers for Disease Control and Prevention:

- Prevention and Control of Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices (ACIP) — United States, 2014–15 Influenza Season accessed at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6132a3.htm?s_cid=mm6132a3_w
- Antiviral Agents for the Treatment and Chemoprophylaxis of Influenza available at http://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm
- Opening and Mixing Tamiflu® Capsules with Liquids if Child Cannot Swallow Capsules http://www.cdc.gov/flu/antivirals/mixing_tamiflu_qa.htm
- Influenza Antiviral Medications: A Summary for Clinicians March 2014- 2015 influenza season: accessed at http://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm
- Treatment- Antiviral drugs accessed at http://www.cdc.gov/flu/antivirals/index.htm
- Guidance for the Prevention and Control of Influenza in the Peri- and Postpartum Settings accessed at http://www.cdc.gov/flu/professionals/infectioncontrol/peri-post-settings.htm
- Centers for Disease Control and Prevention (CDC, Atlanta): http://www.cdc.gov/flu/index.htm

Public Health England:

- Pharmacological treatment and prophylaxis of influenza. Version 1.7; 12 January 2011 http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1287147812045
- PHE guidance on use of antiviral agents for the treatment and prophylaxis of influenza : Version reviewed November 2014.Accessed at https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/370673/AV_full_guidance.pdf

Additional information is available on the following websites:

- NICD-NHLS Website: www.nhls.ac.za then follow link to NICD,
- Department of Health Website: www.doh.gov.za
- World Health Organization Website: http://www.who.int/topics/influenza/en/
- U.S food and drug food and drug administration. http://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/021246Orig1s045_021087Orig1s062_tamiflu_toc.cfm

- Recommendations pertaining to the use of viral vaccines: Influenza 2016 has been published in the February 2016 edition of the South African Medical Journal (access at http://samj.org.za/index.php/samj/article/view/10586

Further questions from health professionals can be addressed to:

- The NICD Hotline - 082 883 9920 ***strictly for use by health professionals only***

7 Appendix 1: Home care guidance: healthcare workers' directions to patients/caregivers

Home Care Guidance: healthcare workers' directions to patients/caregivers

1. You will probably be sick for several days with fever and respiratory symptoms.
2. Take Medications as Prescribed:

- Take all of the antiviral medication as directed (where applicable).
- Continue to cover your mouth and nose when you cough and wash your hands often (even when taking antiviral medications), to prevent spreading influenza to others.
- Visit the clinic/GP if you experience any side effects; i.e. nausea, vomiting, rash, or unusual behaviour.
- Take medications for symptom relief as needed for fever and pain such as paracetamol or ibuprofen. These medicines do not need to be taken regularly if your symptoms improve.
- Do not give aspirin (acetylsalicylic acid) or products that contain aspirin to children or teenagers 18 years old or younger.
- Do not give aspirin or NSAIDs to pregnant women.
- Children should not be given over-the-counter cold medications without first consulting a healthcare worker.

3. Seek Emergency Care:

If your child experiences any of the following:

- Fast breathing or difficulty breathing
- Bluish or grey skin colour
- Not drinking enough fluids
- Severe or persistent vomiting
- Not waking up or not interacting
- Being so irritable that the child does not want to be held
- Flu-like symptoms improve but then return with fever and worse cough

In adults, emergency warning signs that need urgent medical attention include:

- Difficulty breathing or shortness of breath
- Pain or pressure in the chest or abdomen
- Sudden dizziness
- Confusion
- Severe or persistent vomiting
- Flu-like symptoms improve but then return with fever and worse cough

4. Follow These Home Care Recommendations:

- Stay home for 7 days after your symptoms begin
- Drink clear fluids (such as water, broth, sports drinks, electrolyte beverages for infants) to keep from being dehydrated.
- Dishes etc. can be washed with hot soapy water.
- Throw away tissues and other disposable items used by the sick person in the rubbish bin. Wash your hands after touching used tissues and similar waste.
- Have everyone in the household wash hands often with soap and water, especially after coughing or sneezing. Alcohol-based hand cleaners are also effective.
- Avoid touching your eyes, nose and mouth.
- Continue with medication for chronic diseases as prescribed (e.g. ART, TB treatment).

8 Appendix 2: Management of patients with suspected or proven influenza virus infection

Category	Clinical Definition	Treatment	Diagnostic Tests
Uncomplicated Influenza-like illness (ILI)	ILI (Influenza-like Illness) Influenza presenting with fever, coryza, generalised symptoms (headache, malaise, myalgia, arthralgia) and sometimes gastrointestinal symptoms, but without any features of complicated influenza.	**NO RISK FACTORS PRESENT:** ■ Symptomatic treatment with paracetamol ± alternative analgesia. ■ Avoid aspirin in children and adolescents ≤18 years (risk of Reye Syndrome). ■ Avoid aspirin and NSAIDs in pregnant women	NOT for routine diagnostic testing
		RISK FACTORS PRESENT ■ Oseltamivir orally twice per day for 5 days‡	Consider testing if it may change clinical management
Complicated or severe influenza	Influenza requiring hospital admission and/or with symptoms and signs of lower respiratory tract infection (hypoxaemia, dyspnoea, lung infiltrate), central nervous system involvement and/or a significant exacerbation of an underlying medical condition ■ Other conditions/clinical presentations requiring hospital admission for clinical management (including secondary bacterial pneumonia with influenza, most commonly *Streptococcus pneumoniae*, *Staphylococcus aureus* and *Streptococcus pyogenes*).	■ **Treatment should be started as soon as any of the clinical criteria are met**†. ■ **URGENT EARLY REFERRAL to hospital for supportive care and assessment** ■ Oseltamivir orally twice per day for 5 days (consider prolonged duration for critically ill patients). ■ Antibiotics – to cover *S. aureus*, *S. pneumoniae* and *S. pyogenes* (e.g. co-amoxiclav) ■ Early oxygen supplementation and close monitoring of oxygen saturation. ■ Ensure adequate hydration and monitor renal function.	Send nasopharyngeal /throat swabs for influenza testing if it will change clinical management. Testing for influenza should NOT delay administration oseltamivir when clinically indicated

*****Risk factors: infants and young children (particularly <2 years of age); pregnant women (including the post-partum period); persons of any age with chronic diseases including: pulmonary diseases (e.g. asthma, tuberculosis, COPD), cardiac diseases (e.g. congestive cardiac failure), metabolic disorders (e.g. diabetes), renal disease, hepatic disease, certain neurological conditions, (neuromuscular, neurocognitive and seizure disorders), haemoglobinopathies, immunosuppression (e.g. HIV, immunosuppressive medication or malignancy), persons ≤18 years receiving chronic aspirin therapy, persons aged ≥65 years, persons who are morbidly obese (BMI ≥40).

‡ All attempts should be made to start oseltamivir within the first 48 hours of symptoms.

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