

# ASID/TSANZ guidelines: treatment and prevention of H1N1 influenza 09 (human swine influenza) with antiviral agents

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Since the initial reports of H1N1 influenza (human swine influenza; caused by influenza A/2009/H1N1/swl) in Mexico and the United States in mid April 2009, many thousands of cases have been reported worldwide. At the time of writing, community transmission is becoming established in many areas in Australia, but the number of reported cases is likely to be an underestimate of the true incidence due to policies for testing.

These guidelines provide advice to clinicians on the use of antiviral agents for H1N1 influenza 09, drawing on studies of seasonal and H5N1 (avian) influenza, emerging data on H1N1 influenza, and previous guidelines.<sup>1-4</sup> Anti-influenza drugs are not usually available on the Pharmaceutical Benefits Scheme, but the national stockpile has been released for treatment and prophylaxis during this outbreak.

## Process of guideline development

Because of the rapidly evolving situation, an expedited process was undertaken to develop these guidelines. One of us (ACC) reviewed the literature and formulated guidelines with substantial input from the other authors, with review by the Guidelines Committee and Executive Council of the Australasian Society for Infectious Diseases (ASID). ASID members were invited to comment; the authors responded to all comments received. The Swine Influenza Task Force of the Thoracic Society of Australia and New Zealand (TSANZ) were invited to review the guidelines. These guidelines represent a joint position statement of the ASID and the TSANZ.

## Case recognition and diagnosis

The case definition of H1N1 influenza 09 is likely to change depending on the extent of community transmission worldwide and in Australia. A current case definition can be found on the Australian Government Department of Health and Ageing website.<sup>5</sup> In areas with established community transmission, patients presenting with an acute respiratory illness are considered to have H1N1 influenza 09. In areas where community transmission has not been established, patients presenting with an acute respiratory illness should be tested for H1N1 influenza 09. At the time of writing, an acute respiratory illness is defined as a person presenting with a fever ( $\geq 38^{\circ}\text{C}$  or a good history) with cough and/or sore throat.

The clinical profile of H1N1 influenza 09 appears to be similar to that of seasonal influenza, for which fever, cough and fatigue are the most common symptoms.<sup>6</sup> In the first school outbreak of H1N1 influenza 09 in New York, symptoms associated with H1N1 influenza were cough (98%), subjective fever (96%), fatigue (89%), headache (82%), sore throat (82%), runny nose (82%), chills (80%), and muscle aches (80%); 95% of patients had a fever and cough and/or sore throat.<sup>7</sup> Nausea (55%), abdominal pain (50%), diarrhoea (48%), shortness of breath (48%), and joint pain (46%) were also reported.<sup>7</sup> A striking feature of current reports is the young age of patients; the median age of patient death in

## ABSTRACT

- To date, there have been thousands of cases of H1N1 influenza 09 (human swine influenza) worldwide, with established community transmission in parts of Australia.
- Timely diagnostic tests can enable targeted antiviral treatment early in the course of the pandemic. Rapid antigen tests will be less useful once the pandemic is established.
- Recommendations for use of antiviral treatment for influenza:
  - Neuraminidase inhibitors (oseltamivir and zanamivir) are the antiviral agents of choice for H1N1 influenza 09.
  - In otherwise healthy children and adults with confirmed or suspected influenza, antiviral treatment is of greatest benefit when given within 48 hours of symptom onset.
  - Treatment should be prioritised for patients with risk factors for severe disease, such as older people (> 65 years), pregnant women, patients with chronic disease (eg, asthma, cardiorespiratory disease, diabetes and renal failure) or immunosuppression, and young children.
  - Antiviral treatment can be given to children as young as 1 year. However, animal studies suggest central nervous system accumulation of oseltamivir in infants < 1 year. Parents should be informed of the possibility of uncommon neuropsychiatric adverse events among children.
  - Antiviral treatment should be offered to pregnant women with suspected or confirmed influenza because of the risk of severe disease in this group; there is limited evidence suggesting safety during pregnancy.
  - Antiviral treatment should be given to hospitalised patients with severe influenza infection (especially pneumonia), even > 48 hours after symptom onset. Antibiotics should be given to such patients according to established guidelines for community-acquired pneumonia.
- Recommendations for use of antiviral prophylaxis:
  - Antiviral prophylaxis can be given to health care workers and close contacts of patients with influenza following exposure, and to residents of institutions to terminate outbreaks. Contacts not provided with prophylaxis should have access to early treatment with antiviral agents.
  - Long-term prophylaxis can be given to "first responder" health care workers for durations of up to 6 weeks for oseltamivir and 4 weeks for zanamivir. Use of antiviral prophylaxis for these groups should be in the context of agreement to use the national stockpile.

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**1 Factors to consider in deciding on likelihood of H1N1 influenza 09 (human swine influenza) infection**

**Current epidemiology: "pre-test probability"**

- Pandemic phase
  - Delay — no/few cases in Australia
  - Contain — transmission in specific settings or regions
  - Sustain — widespread cases in some areas
  - Protect — widespread transmission
- Known history of contact with a person with influenza
- Known history of travel to countries/region with established transmission

**Clinical scenario**

- Clinical case definition — fever, cough and/or sore throat (with epidemiological risk factors where appropriate)
- Results of rapid testing for influenza
- Results of confirmatory testing for influenza ◆

**2 Factors to consider in deciding on likely benefits of treatment for H1N1 influenza 09 (human swine influenza) infection**

**Established complications**

- Hospitalised patients
- Patients with respiratory compromise
- Patients with pneumonitis or secondary bacterial pneumonia

**High risk of complications**

- Pregnant women
- Patients with morbid obesity
- Indigenous Australians
- Patients with chronic respiratory illness; other comorbidities (see Box 3)

**Potential for transmission to others**

- Health care workers and first responders (eg, paramedics)
- Household contact or carer of high-risk patient

**Low risk of complications**

- Healthy adults

**Low likelihood of benefit**

- Presentation > 48 hours after onset of illness
- High prevalence of circulating influenza strains with resistance to neuraminidase inhibitors

**Potential risks of treatment**

- Infants < 1 year ◆

Mexico was 31 years, and 60% of hospitalised patients in California were aged under 18 years.<sup>2</sup> Comorbidities were reported in 64% of hospitalised patients in California and 46% of deaths in Mexico. Current data suggest that the case-fatality ratio appears to be low outside Mexico (<0.2%).

Studies have demonstrated the clinical difficulty in differentiating patients with influenza from those with other respiratory viral infections. Thus, the likelihood of influenza among patients with acute respiratory infections will depend on the prevalence of influenza relative to other respiratory viruses. In Australia, about 40% of patients meeting a case definition of influenza-like illness have laboratory-confirmed seasonal influenza.<sup>8</sup> A systematic review of studies of the sensitivity and specificity of clinical symptoms in seasonal influenza concluded that fever, malaise and cough were more common among patients older than 60 years with confirmed seasonal influenza than those with other viral infections, but no other symptoms or combination of symptoms were reliable predictors for all age groups.<sup>9</sup>

In regions without established transmission, patients presenting with a significant influenza-like illness should have respiratory tract sampling to confirm the diagnosis of influenza virus infection. In areas where transmission is established, testing is only recommended for patients with severe disease, those at risk of complications, and health care workers or other patients who work with vulnerable populations. Health care workers performing nose swabs or other high-risk aerosol-generating procedures (eg, suctioning, bronchoscopy or intubation) should use a particulate respirator (N95, P2 mask or equivalent), eye protection, impervious gowns and gloves, and, where possible, carry out the procedure in a negative pressure room. Personal protective equipment removal must be conducted with care, as there is a risk of self-inoculation. The use of a combined nose-throat swab is recommended, with studies demonstrating a high sensitivity with "flocked" swabs comparable with nasopharyngeal aspirate.<sup>10-12</sup> The use of nasopharyngeal aspirate is not recommended due to the risk to staff, although it may be more sensitive than nose or throat swabs.<sup>13</sup>

The definitive diagnosis of H1N1 influenza 09 can only be made by nucleic acid testing using influenza A and influenza A H1N1/2009/swl-specific primers. Antigen detection assays (including rapid or point-of-care, and immunofluorescence) will differentiate between influenza A and B only; a positive test for influenza A will

not differentiate seasonal influenza (H3 or H1) from H1N1 influenza 09 infection.

The sensitivity of antigen detection assays for detecting H1N1 influenza 09 is not yet known. Commercial rapid antigen tests that use throat or nose swabs are available, and can obtain a result within 15–30 minutes. The rapid tests generally have a sensitivity of 60%–80% compared with viral culture, so a negative test does not exclude influenza.<sup>9</sup> The sensitivity of these tests suggests that the rapid antigen tests are less useful where the pre-test probability is high (ie, during the "sustain" phase of an established pandemic). Should community transmission of H1N1 influenza 09 become established in Australia, rapid differentiation of H1N1 influenza 09 from seasonal influenza strains may not be possible on clinical grounds or using rapid testing. Specimens for viral nucleic acid detection and culture at reference laboratories should be taken for epidemiological surveillance and to monitor for drug resistance.

The decision to treat an individual patient, particularly before the results of confirmatory testing are available, depends on three factors:

- An assessment of the likelihood of influenza (Box 1), based on the known prevalence of infection in the region, a history of contact and the characteristics of the illness.
- An assessment of the likely benefits of treatment (Box 2), based on the presence of established complications, comorbidities and risk factors (Box 3), and the time from the onset of illness.
- The availability of antiviral drugs, and public health policies regarding distribution of the national stockpile.

**Neuraminidase inhibitors: oseltamivir and zanamivir**

The two agents effective against influenza are oral oseltamivir and inhaled zanamivir. These agents, which inhibit viral neuramini-

**3 Patients at risk of complications from influenza infection\***

- Pregnant women
- Aboriginal and Torres Strait Islander people
- Patients with:
  - chronic respiratory disease (including asthma and chronic obstructive pulmonary disease);
  - cardiac disease;
  - morbid obesity;
  - chronic diseases (eg, diabetes, chronic metabolic diseases, chronic renal failure, haemoglobinopathies);
  - chronic neurological disorders; or
  - impaired immunity, including HIV infection
- Homeless people
- Residents of nursing homes and long-term care facilities
- Children aged 6 months – 10 years on long-term aspirin therapy
- Older people (> 65 years)
- Children < 5 years

\* Adapted from the *Australian immunisation handbook*.<sup>14</sup> ◆

**4 Dose recommendations for treatment of influenza**

Treatment	Dose, interval, duration
<b>Oseltamivir</b>	
Adults; children > 13 years	75 mg, twice daily orally, 5 days
Renal impairment*	75 mg, daily orally, 5 days
Children aged 1–13 years	
< 15 kg	30 mg, twice daily, 5 days
15–23 kg	45 mg, twice daily, 5 days
23–40 kg	60 mg, twice daily, 5 days
> 40 kg	75 mg, twice daily, 5 days
<b>Zanamivir</b>	
Adults	10 mg (2 inhalations), twice daily, 5 days
Children > 5 years	10 mg (2 inhalations), twice daily, 5 days

\* Creatinine clearance, 10–30 mL/min. ◆

**5 Dose recommendations for prophylaxis against influenza**

Prophylaxis	Dose, interval, duration
<b>Oseltamivir</b>	
Adults; children > 13 years	75 mg, daily, 10 days
Renal impairment*	75 mg, alternate days, 10 days
Children aged 1–13 years	
< 15 kg	30 mg, daily, 10 days
15–23 kg	45 mg, daily, 10 days
23–40 kg	60 mg, daily, 10 days
> 40 kg	75 mg, daily, 10 days
<b>Zanamivir</b>	
Adults	10 mg (2 inhalations), daily, 10 days
Children > 5 years	10 mg (2 inhalations), daily, 10 days

\* Creatinine clearance, 10–30 mL/min. ◆

dase, are approved for use in Australia for the treatment and prevention of influenza A and B infection. Dose recommendations for treatment are summarised in Box 4 and for post-exposure prophylaxis in Box 5.

Both agents are generally well tolerated. Zanamivir has been associated with cough, bronchospasm and dyspnoea in some patients, but appears to be safe in patients with chronic respiratory diseases.<sup>15</sup> Inhaled zanamivir may be difficult to administer to small children and older adults, as they may have difficulty with inhaler technique. Patients should be warned about the possibility of increasing dyspnoea, and patients with chronic respiratory diseases should have access to a fast-acting bronchodilator. Oseltamivir is associated with transient nausea, vomiting and abdominal pain in 2%–10% of patients;<sup>16</sup> these side effects may be mitigated by administration with food. There are no studies of repeat dosing in the event of vomiting; in the absence of evidence, it is reasonable to repeat the dose (with food) if vomiting has occurred within 30 minutes of administration or after this time if the capsule is visible in the vomitus. In the event of further vomiting with repeated doses, administration with food and/or an antiemetic, use of the suspension rather than the capsule, or use of zanamivir may be considered. Oseltamivir is renally excreted; a dose adjustment is required for patients with creatinine clearance between 10 and 30 mL/min. Oseltamivir is contraindicated for patients on dialysis. Zanamivir can be used in patients with renal failure without dose adjustment.

Resistance to oseltamivir has been noted in a high proportion of seasonal human H1N1 strains in Australia and elsewhere since 2007,<sup>17</sup> but not in H1N1 influenza 09. In 2008, seasonal H1N1 strains were a minority of the 805 Australian influenza strains collected and analysed by the World Health Organization Collaborating Centre in Melbourne.<sup>18</sup> There are reports of resistance developing in patients while being treated for severe H5N1 (avian) influenza associated with poor outcomes.<sup>19</sup> It appears that seasonal H1N1 strains resistant to oseltamivir are at least as virulent in causing complications as non-resistant strains.<sup>20</sup> Most oseltamivir-resistant seasonal H1N1 strains retained susceptibility to zanamivir.<sup>21</sup> Thus, unless evidence emerges of widespread resistance in H1N1 influenza 09, both antiviral agents would be expected to be effective for the empiric treatment of influenza-like illness due to presumed H1N1 influenza 09 or seasonal influenza strains where indicated.

Indications for use of oseltamivir and zanamivir for H1N1 influenza 09 are detailed below and summarised in Box 6.

**Treatment of H1N1 influenza 09 in otherwise healthy adults**

There are no current data on the efficacy of neuraminidase inhibitors in H1N1 influenza, but in-vitro testing suggests that resistance mutations are not present in H1N1 influenza 09.<sup>22</sup> Data from studies of seasonal influenza suggest that patients with confirmed influenza treated within 36–48 hours of symptom onset had a 1–2-day shorter duration of symptoms and a shorter time to return to normal activity.<sup>23,24</sup> A greater reduction in the duration of symptoms was observed in patients who commenced oseltamivir earlier.<sup>25,26</sup> Treatment of otherwise well health care workers is generally indicated to reduce the time off work, but depends on public health and hospital policies. Use of

oseltamivir was also associated with a reduction in the incidence of antibiotic use and lower respiratory tract infection.<sup>27</sup> Although it is not known whether treatment reduces overall infectivity, treatment is associated with reduced viral load (although the duration of viral shedding is not changed in all studies) and a shorter duration of symptoms (including coughing).<sup>16,24,28,29</sup> There is limited epidemiological evidence of a reduction in transmission in households associated with treatment in an analysis of the prophylaxis trials.<sup>30</sup>

### Treatment of H1N1 influenza 09 in infants and children

Children younger than 5 years, and those with comorbidities and immunosuppression, are at increased risk of complications. Oseltamivir has been shown to be effective for seasonal influenza in children as young as 1 year,<sup>31</sup> with reductions in the duration of symptoms, complicating otitis media,<sup>32</sup> and asthma exacerbations.<sup>33</sup> An oral suspension of oseltamivir is available for children; this may be administered with food to improve palatability. If the suspension is not available, capsules may be opened to obtain an age-appropriate dosage. Use of the inhaler device limits the use of zanamivir for young children.

There are limited safety data for infants aged under 12 months.<sup>34,35</sup> Studies in juvenile rats have raised concerns that oseltamivir may accumulate in the central nervous system.<sup>36</sup> The US Food and Drug Administration has approved the use of oseltamivir in infants aged under 1 year under an Emergency Use Authorization.<sup>37</sup> In children aged under 1 year, the recommended dose of oseltamivir is 2 mg/kg/dose, rounded up to the nearest 0.25 mL gradation, twice daily using a standard graded 3 mL syringe (personal communication, Kay Hynes, Pharmacy Department, Royal Children's Hospital, Melbourne, Vic). The decision to treat must balance the perceived benefits of treatment against the theoretical toxicity concerns. Neuraminidase inhibitors in infants aged under 3 months would only be indicated in critically unwell infants.

There are reports of oseltamivir-associated behavioural disturbances in children in Japan and Korea.<sup>38</sup> Large company-sponsored epidemiological studies in the US have not found an increased association between oseltamivir use and neuropsychiatric events.<sup>39,40</sup>

### Treatment of H1N1 influenza 09 in groups at risk of complications

Meta-analyses suggest that treatment with oseltamivir reduced the incidence of lower respiratory tract complications requiring antibiotic treatment; the absolute benefit was greatest in "at-risk" patients, defined as patients aged over 65 years and patients with respiratory or cardiac compromise.<sup>24,27</sup> An overall reduction in the rate of hospitalisations was observed in patients treated with oseltamivir. A small observational series found that oseltamivir reduced the progression to pneumonia in patients with influenza infection following haematopoietic stem cell transplantation.<sup>41</sup> Older patients in institutions (eg, nursing homes) are at particular risk because of comorbidities and the efficiency of transmission of influenza in closed settings. Where patients with influenza are known to have been present, exposed patients and staff should have access to prophylaxis or early treatment for presumed influenza.

Influenza is associated with exacerbations of asthma, and hospitalisation rates from influenza are higher in children with asthma.<sup>42</sup>

Longitudinal studies suggest that influenza decreases forced expiratory volume in 1 second by a mean of 30% by the second day, with recovery taking up to 7–10 days.<sup>43</sup> A trial of oseltamivir did not show a significant decrease in the duration of illness or improvement in symptom scores, but it did show a small improvement in the rate of recovery of lung function.<sup>33</sup> Of 30 patients hospitalised in California with H1N1 influenza 09, 19 had underlying medical problems, including chronic respiratory disease, immunosuppression, chronic cardiac disease, diabetes and obesity.<sup>44</sup>

Limited evidence suggests that pregnant women should be offered neuraminidase inhibitors for treatment of influenza. Oseltamivir and zanamivir are in the Australian Drug Evaluation Committee category B1. A review of 232 pregnancies with maternal exposure to oseltamivir (including 12 with fetal disorders) did not find evidence suggesting that oseltamivir was associated with adverse pregnancy or fetal outcomes.<sup>45</sup> Reports of severe H1N1 influenza 09 in pregnant women have prompted the US Centers for Disease Control and Prevention to recommend treatment of pregnant women with neuraminidase inhibitors; of 20 known cases of H1N1 influenza 09 in pregnancy, three patients required hospitalisation, and one of these died.<sup>46</sup> Pregnant women with influenza (or following exposure to patients with influenza) require close clinical monitoring. The Communicable Diseases Network Australia has also provided advice supporting this recommendation.

### Treatment of severe H1N1 influenza 09

Although evidence of efficacy is lacking in patients with severe influenza, most clinicians agree that treatment is indicated where viral replication may be contributing to illness in severely unwell patients. Limited observational data suggest that hospitalised patients presenting over 48 hours after onset of symptoms may still benefit,<sup>47</sup> although efficacy is likely to be related to earlier administration of antiviral medications. Therefore, it may be reasonable to offer antiviral therapy to patients with severe influenza or influenza pneumonia, even if they present later than 48 hours after symptom onset. Case-by-case assessment is recommended. Efficacy is likely to fall rapidly for each day beyond the recommended 48-hour threshold.

The efficacy of neuraminidase inhibitors in severe influenza is supported by experience with treatment of H5N1 (avian) influenza with oseltamivir, where survival was associated with viral suppression by Day 3, compared with ongoing detection of viral replication in patients who died.<sup>19,48</sup> Additionally, animal models of H5N1 (avian) influenza suggest that oseltamivir is protective against mortality. It is not known whether the extrapulmonary virus detected in severe H5N1 influenza reflects extrapulmonary replication; if so, oseltamivir may have a theoretical advantage over inhaled zanamivir.

Oseltamivir is only available for oral administration; intravenous preparations of neuraminidase inhibitors (eg, peramivir) are not generally available. Limited data suggest that absorption in critically ill patients is adequate, with similar pharmacokinetics to healthy patients.<sup>49</sup> Doses of up to 500 mg twice daily have been tolerated in healthy adults in clinical trials.<sup>69</sup> There is concern that the risks of underdosing (particularly in patients with poor gastric perfusion, altered volumes of distribution, or obesity) may result in poor outcomes.<sup>70</sup> A loading dose of oseltamivir 150 mg should be administered nasogastrically for critically unwell patients with severe influenza, and intensive care patients with normal renal

## POSITION STATEMENT

### 6 Indications for antiviral treatment and prophylaxis for H1N1 influenza 09 (human swine influenza) infection, depending on likelihood of benefit and stage of pandemic

Pandemic phase	Delay	Contain	Sustain	Protect
Epidemiological setting	Little or no community transmission; cases identifiable via exposure history	Limited community transmission; cases not identifiable via exposure history	Community transmission in some regions	Widespread community transmission
<b>Treatment</b>				
Patients with established complications	Clinically presumed or laboratory-confirmed	Clinically presumed or laboratory-confirmed	Clinically presumed or laboratory-confirmed	Clinically presumed or laboratory-confirmed
Groups at risk of complications*	Clinically presumed or laboratory-confirmed. Consider treatment > 48 h after onset if severe or not improving	Clinically presumed or laboratory-confirmed. Consider treatment > 48 h after onset if severe or not improving	Clinically presumed or laboratory-confirmed. Consider treatment > 48 h after onset if severe or not improving	Clinically presumed or laboratory-confirmed. Consider treatment > 48 h after onset if severe or not improving
Health care workers, carers for patients at risk of complications within 48 h of onset of illness	Clinically presumed or laboratory-confirmed	Clinically presumed (if appropriate exposure history) or laboratory-confirmed	Clinically presumed or laboratory-confirmed	Clinically presumed or laboratory-confirmed
Otherwise healthy adults and children > 5 y within 48 h of onset of illness	Clinically presumed or laboratory-confirmed	Laboratory-confirmed	Clinically presumed (depending on rationing policy and virulence)	Not generally indicated
Infants < 1 y	Depends on clinical scenario	Depends on clinical scenario	Depends on clinical scenario	Depends on clinical scenario
Low likelihood of benefit (> 48 h after presentation, known high prevalence of resistance)	Not indicated, unless severe infection present. Consider zanamivir if oseltamivir-resistant	Not indicated, unless severe infection present. Consider zanamivir if oseltamivir-resistant	Not indicated, unless severe infection present. Consider zanamivir if oseltamivir-resistant	Not indicated, unless severe infection present
<b>Prophylaxis following exposure</b>				
Groups at risk of complications*	Indicated	Indicated	Indicated (depending on rationing policies)	Not generally indicated, except immunosuppressed patients and closed communities
Health care workers, carers for patients with comorbidities	Indicated	Indicated	Indicated (depending on policy for national stockpile)	Not generally indicated (depending on hospital policy)
Healthy adults and children > 5 y within 48 h of exposure	Indicated	Indicated	Not indicated (depending on rationing policy and virulence)	Not indicated
Children < 1 y	Not generally indicated	Not generally indicated	Not generally indicated	Not generally indicated
Low likelihood of benefit (> 48 h after exposure)	Consider up to 7 days after exposure to prevent transmission	Depends on observed incubation period and public health policy	Consider early treatment if symptoms develop	Not indicated

\* Such as pregnant women, patients with comorbidities, or immunosuppression, and Indigenous Australians (Box 3). ◆

function should be given oseltamivir 75–150mg nasogastrically twice daily. In patients undergoing continuous veno-venous haemofiltration, the sieving coefficient is 1; thus the ultrafiltration rate approximates the glomerular filtration rate.<sup>71</sup> The duration of treatment will depend on the clinical response; a 10-day course may be required, and a longer course may be indicated when ongoing influenza pneumonitis is suspected.

Antibiotic treatment should not be given routinely for influenza-like illness, but antibiotic treatment should follow established national guidelines for treatment of community-acquired pneumonia. The relative contribution of primary influenza pneu-

monitis and secondary bacterial pneumonia to mortality in pandemic influenza is controversial.<sup>50</sup> In the 1968 influenza pandemic, a threefold rise in pneumonia due to *Staphylococcus aureus* was observed, which accounted for 26% of bacteriologically confirmed cases.<sup>51</sup> In contrast, ongoing viral replication appears to be predictive of mortality in cases of H5N1 (avian) influenza.<sup>19,48</sup> A review of mortality in Mexico found a rapid progression to acute respiratory distress syndrome, with a low rate of bacterial isolation.<sup>2</sup> Initial autopsy studies have been consistent with acute respiratory distress syndrome secondary to viral pneumonia. Until further data are available, patients with

pneumonia associated with influenza should have blood and sputum cultures and be treated with neuraminidase inhibitors and antibiotics for community-acquired pneumonia. Antibiotics active against *S. aureus* should be considered for patients with severe pneumonia.

### Prevention of H1N1 influenza 09 in health care workers and close contacts

The use of infection control procedures, including personal protective equipment, is recommended to protect staff.<sup>52</sup> Considerable evidence from previous pandemics suggests that droplet (generally up to 1–2 m) and contact spread (both patient-to-patient, and via fomites) are the predominant modes of transmission, with some evidence possibly consistent with small droplet, airborne transmission over longer distances, particularly in low-humidity environments.<sup>53</sup> Diarrhoea has been reported in around half of patients with H1N1 influenza 09; all bodily fluids should be regarded as potentially infective until further data are available.

All health care workers and at-risk groups should minimise their exposure risk to patients with influenza-like illness as much as possible by adhering to current infection control guidelines. In particular, patients with influenza symptoms or unidentified febrile respiratory illness should use spacers if required and avoid nebulisers where possible. Where this is not practical or possible, the nebuliser should be used in a well ventilated space, with 1 m minimum distance between beds designed to minimise staff and patient exposure.<sup>54</sup> Nebulised antibiotics in those with bronchiectasis should be withheld and intravenous preparations used for respiratory virus-associated exacerbations until found to be clear of influenza. Other respiratory invasive procedures (suction, intubation, positive pressure ventilation) were associated with significant risk of increased transmission of severe acute respiratory syndrome,<sup>55-57</sup> and should be undertaken with suitable infection control precautions to minimise droplet and aerosol transmission of virus.

Antiviral prophylaxis may potentially be recommended to reduce morbidity in staff and the risk of transmission in two settings:

- As pre-exposure prophylaxis (eg, for paramedics consistently exposed to patients where the use of personal protective equipment is not practical).
- As post-exposure prophylaxis for health care workers or close contacts following an unprotected exposure to a patient with H1N1 influenza 09. This includes carers of immunosuppressed patients and contacts of patients in institutional settings, such as nursing homes, schools and hospitals, to prevent or terminate outbreaks.

Studies of long-term prophylaxis have enrolled healthy adults, residents of nursing homes or participants at high risk of complications for 4–6 weeks, and have demonstrated that use of neuraminidase inhibitors was associated with 83%–91% protective efficacy against influenza.<sup>58-60</sup> The use of long-term antiviral prophylaxis for a selected cohort of health care workers (eg, paramedics, emergency department staff) will depend on policies for the use of the national stockpile of antiviral agents.

Studies of post-exposure prophylaxis for 10 days have enrolled patients within 36–48 hours of exposure to a household contact, and have demonstrated a protective efficacy of 78%–89% compared with expectant treatment with the onset of symptoms.<sup>61-64</sup>

Additionally, prophylaxis for non-infected residents has also been used to terminate outbreaks of influenza in institutional settings in observational studies.<sup>65-67</sup>

There is insufficient evidence to definitively guide the use of antiviral prophylaxis after more than 48 hours post-exposure; however, this threshold has probably been adopted due to the short incubation period of seasonal influenza — the incubation period in newly emerged influenza strains may be up to 7 days. Health care workers and household contacts not provided with prophylaxis should be counselled on their need to stay away from work if they become unwell and have access to early treatment with antiviral treatment where indicated.

### Prevention of H1N1 influenza 09 in travellers

The decision to supply neuraminidase inhibitors not subsidised by the Pharmaceutical Benefits Scheme to travellers where community transmission is widespread must be made on an individual basis. Travellers should be given advice regarding risk-reduction strategies (including deferment of travel if possible), the lack of specificity of a clinical definition of influenza-like illness (particularly if seasonal influenza is also circulating) and potential adverse events.

### Other interventions

Adamantanes (amantadine or rimantadine) are not recommended, as testing of H1N1 influenza 09 strains have demonstrated in-vitro resistance to these agents. They are also commonly associated with neuropsychiatric side effects.

Although vaccination against seasonal influenza is not believed to be effective against H1N1 influenza 09 strains<sup>68</sup> and no new H1N1 vaccine for this strain is yet available, vaccination is still suggested for at-risk groups to protect individuals against seasonal influenza and because seasonal influenza may complicate case detection, particularly in health care workers. Current recommendations for routine seasonal influenza vaccine include adults aged over 65 years (and Indigenous Australians aged over 15 years), patients with chronic illness (including those with asthma, cardio-respiratory disease, diabetes and renal failure) or who are immunosuppressed, pregnant women, residents of nursing homes and health care workers.

### Updated information

We acknowledge that the evidence on which these recommendations are based is rapidly changing. In particular, estimates of disease severity and case fatality, and risk factors for severity are poorly defined at present and may influence clinical decision making. We therefore include some resources for further information:

- Updates to these clinical guidelines will be posted on the ASID (<http://www.asid.net.au>) and TSANZ websites (<http://www.thoracic.org.au>).
- Australian resources for pandemic influenza, including links to clinical and infection control guidelines (<http://www.flupandemic.gov.au>) and current information on the H1N1 outbreak (<http://www.healthemergency.gov.au> and <http://www.influenza-specialistgroup.org.au>).
- For information on accessing personal protective equipment and antiviral medication, see links below:

- <http://www.emergency.health.nsw.gov.au/swineflu/professionals/index.asp> (New South Wales)
- <http://humanswineflu.health.vic.gov.au/practitioners/index.htm> (Victoria)
- [http://www.health.qld.gov.au/swineflu/html/hc\\_resources.asp](http://www.health.qld.gov.au/swineflu/html/hc_resources.asp) (Queensland)
- <http://flu.sa.gov.au/Swineflu/InformationforGPs.aspx> (South Australia)
- [http://www.public.health.wa.gov.au/3/952/3/human\\_swine\\_flu\\_health\\_providers.pm](http://www.public.health.wa.gov.au/3/952/3/human_swine_flu_health_providers.pm) (Western Australia)
- [http://www.pandemic.tas.gov.au/what\\_does\\_it\\_mean\\_to\\_you/health\\_sector](http://www.pandemic.tas.gov.au/what_does_it_mean_to_you/health_sector) (Tasmania)
- [http://www.health.nt.gov.au/H1N1\\_Influenza/General\\_Information\\_Resources/index.aspx](http://www.health.nt.gov.au/H1N1_Influenza/General_Information_Resources/index.aspx) (Northern Territory)
- <http://health.act.gov.au/c/health?a=da&did=11044035&pid=1242181681> (Australian Capital Territory).

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### Competing interests

Dominic Dwyer has undertaken clinical trials with anti-influenza drugs and new laboratory assays for Roche, GlaxoSmithKline and other companies. Jim Buttery has served as an investigator or on data-safety monitoring committees for influenza vaccine trials for Wyeth Vaccines and CSL. Paul Johnson has worked as a consultant for Biota, but not regarding antiviral drugs.

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