



Acute Uncomplicated Influenza



Previously Healthy*

- Jennifer (age 36)
- Project manager
- Has two (2) children



High Risk†

- Frank (age 65)
- Construction foreman
- Has diabetes and COPD



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Case Study

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Influenza

Burden of Influenza

Transmission of Influenza

Laboratory Tests for Influenza

Alleviation of Influenza Symptoms

High-risk Populations†

Influenza-related Complications

Improvement of Influenza Symptoms

*Refers to previously healthy, symptomatic outpatient not at high risk for influenza complications; †for influenza-related complications. COPD=chronic obstructive pulmonary disorder.

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CASE DETAILS

- Age 36; Project manager
- Has two boys (aged 3 and 6)
- Woke up with a fever and congestion
- Cases of influenza have been reported at her office



DISEASE COURSE

- Viral testing (RIDT) confirms presence of influenza
- Treated with an antiviral

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Clinical and Economic Burden of Illness



Laboratory Tests for Influenza



Transmission of Influenza



Alleviation of Influenza Symptoms

*Refers to previously healthy, symptomatic outpatient not at high risk for influenza complications
RIDT=rapid influenza diagnostic test.



Seasonal Influenza Has a Significant Clinical and Economic Burden

Clinical Burden of Illness



- Annually, influenza infections occur in **5–20% of the population** in the US¹
- From 2010–2019, the CDC estimates that the **annual clinical burden** of seasonal influenza ranged from²:

9.3–45.0 million
illnesses



4.3–21.0 million
HCP visits



140,000–810,000
hospitalizations



12,000–61,000
deaths



Economic Burden of Illness



- As a result of influenza infection, there are an annual estimated:
- Influenza epidemics are estimated to cost the US economy

17 million *missed work days*³



91 million *missed school days*^{4,*}



≈\$87 billion/year

in illness (but not medically attended), outpatient visits, hospitalizations, mortality, and time lost from work or premature death^{5,†}

*Data from 2012–2013. Statistic from an outside organization. Genentech does not endorse or review the content of external sites; †total cost is the sum of all medical costs, loss of earnings due to lost productivity from illness (for recovered cases), and loss of earnings due to lost productivity from premature death. CDC=Centers for Disease Control and Prevention; HCP=healthcare provider.
1. <http://www.nfid.org/influenza>; 2. <https://www.cdc.gov/flu/about/burden/index.html>; 3. <https://www.cdc.gov/niosh/topics/flu/activities.html>;
4. Walgreens 2013 Flu Impact Report. <https://www.multivu.com/players/English/62923-walgreens-flu-season2013/links/62923-2013-Flu-Impact-Survey-10-11-13.pdf>. Sites accessed February 4, 2020; 5. Molinari NA et al. *Vaccine*. 2007;25:5086-5096.






Laboratory Tests for Influenza

CDC

Recommendation¹

- A positive rapid influenza diagnostic test (RIDT) is likely to indicate influenza infection
- Influenza can be diagnosed based on symptoms and clinical judgment alone

		Test Time	Sensitivity	
	Traditional RIDT	<15 min ²	Moderate ³	Most commonly used test⁴
Antigen detection	Immunofluorescence (IFA, DFA)	1–4 h ²	Variable ^{3,5-7}	
	RT-PCR	1–8 h ²	High ^{3,8*}	
Nucleic acid-based	Rapid Molecular Assay (NAAT)	15–30 min ²	High ⁹	
	Conventional	3–10 d ²	High ³	
Viral cell culture	Rapid	1–3 d ²	High ³	

*Most accurate and sensitive test.

CDC=Centers for Disease Control and Prevention; d=days; DFA=direct fluorescent antibody; h=hours; IFA=indirect fluorescent antibody; min=minutes; NAAT=nucleic acid amplification test; RT-PCR=reverse transcription polymerase chain reaction.

1. <https://www.cdc.gov/flu/symptoms/testing.htm>. Accessed February 3, 2020; 2. <https://www.cdc.gov/flu/professionals/diagnosis/table-testing-methods.htm>.

Accessed February 3, 2020; 3. <https://www.cdc.gov/flu/professionals/diagnosis/overview-testing-methods.htm>. Accessed February 3, 2020; 4. Su S et al. *Influenza Other Respir Virus*. 2016;10:86-90;

5. Nutter S et al. *PLoS ONE*. 2012;7:e33097; 6. Ganzenmueller T et al. *J Med Microbiol*. 2010;69:713-717; 7. Pollock NR et al. *Clin Infect Dis*. 2009;49:e66-e68; 8. Fiore E et al. *MMWR*. 2011;60:1-21;

9. Merckx J et al. *Ann Intern Med*. 2017;167:394-409.



Alleviation of Influenza Symptoms

Seven (7) symptoms are typically associated with influenza¹

- Fever
- Cough
- Sore throat
- Runny/stuffy nose
- Muscular or body aches
- Headaches
- Fatigue

Scoring System²

0	No symptoms
1	Mild
2	Moderate
3	Severe

In a Clinical Trial Setting



Time to Alleviation of Influenza Symptoms

has been used as a clinical outcome to evaluate the efficacy of influenza treatment⁷

Influenza antivirals (eg, NAIs) have been shown to shorten the duration of influenza symptoms³⁻⁶



Antivirals should be administered within the first 48 hours of symptom onset³



Antivirals work on different stages of the viral life cycle such as blocking viral uncoating upon entry into the host cell, preventing viral replication, or blocking release of viral particles from the host cell⁴⁻⁶

NAI=neuraminidase inhibitor.

1. <https://www.cdc.gov/flu/symptoms/symptoms.htm>. Accessed January 30, 2020; 2. Powers JH et al. *PLoS One*. 2018;13(3):e0194180; 3. US Department of Health & Human Services, Centers for Disease Control and Prevention. <https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm>. Accessed February 4, 2020; 4. Li T et al. *Viruses*. 2015;7:4929-4944; 5. Koszalka P et al. *Influenza Other Respir Viruses*. 2017;11:240-246; 6. Noshi S et al. *Antiviral Res*. 2018;160:109-117; 7. Lee J et al. *Yonsei Med J*. 2017;58:778-785.

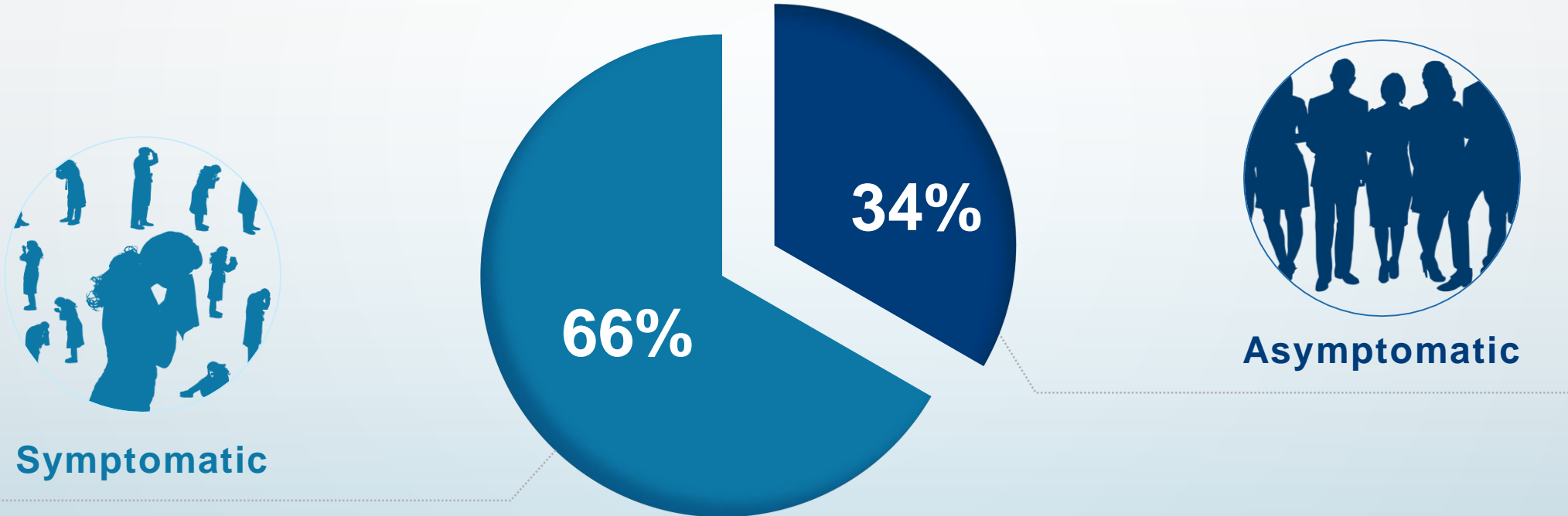
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Transmission of Influenza

Approximately two-thirds of influenza cases are estimated to be transmitted by symptomatic patients and one-third by asymptomatic patients

Estimated proportions of influenza infections caused by symptomatic and asymptomatic people during the 2009 A/H1N1pdm influenza pandemic (England, 2009–2010)



Data may not be representative of the US during typical flu season





CASE DETAILS

- Age 65*
- Construction foreman
- Has diabetes and COPD
- Developed a fever, sore throat, and body aches
- Immediately called primary care provider (PCP) because of existing comorbidities



DISEASE COURSE

- Started on antiviral based on symptoms and PCP clinical judgment

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High-risk Patient Populations



Influenza-related Complications



Improvement of Influenza Symptoms

*Not all elderly patients will develop influenza-related complications, but they are at a greater risk for complications than the general population.¹⁻³
COPD=chronic obstructive pulmonary disease.

1. https://www.cdc.gov/flu/about/disease/high_risk.htm. Accessed January 30, 2020; 2. <https://www.cdc.gov/flu/about/disease/complications.htm>. Accessed January 30, 2020; 3. Mertz D et al. *BMJ*. 2013;347:f5061.



CDC: People at High Risk for Influenza Complications



Individuals with chronic medical conditions^{1,*}

Asthma, diabetes, COPD, etc



Adults aged ≥ 65 years¹



Young children¹

Aged <5 years, but especially aged <2 years



Pregnant women¹

Including up to 2 weeks postpartum



People with a weakened immune system due to disease or medication¹

HIV/AIDS, chemotherapy, etc



Individuals residing in nursing homes or other long-term care facilities¹



American Indians and Alaska Natives¹

Influenza is a serious health threat for high-risk patients²⁻⁴

- Most influenza-related hospitalizations in adults with seasonal influenza are related to exacerbations of underlying diseases²
- Adults aged ≥ 65 years account for the majority of influenza hospitalizations (50–70%[†]) and deaths (70–85%[†]) in the US each year³
- Adults aged ≥ 65 years are especially vulnerable to influenza and related complications due to diminished immune responses⁴



*Includes patients with asthma, neurological and neurodevelopmental conditions, chronic lung disease, heart disease, blood disorders, endocrine disorders, kidney disorders, liver disorders, metabolic disorders, people aged <19 years receiving long-term aspirin therapy, and people with extreme obesity (BMI ≥ 40 kg/m²); [†]CDC estimated occurrence.

AIDS=acquired immunodeficiency syndrome; BMI=body mass index; CDC=Centers for Disease Control and Prevention; COPD=chronic obstructive pulmonary disease; HIV=human immunodeficiency virus.

1. https://www.cdc.gov/flu/about/disease/high_risk.htm. Accessed January 21, 2020; 2. Ipson MG et al. *J Infect Dis.* 2010;201:1654-1662; 3. <https://www.cdc.gov/flu/toolkit/long-term-care/importance.htm>. Accessed January 21, 2020; 4. Keilich SR et al. *Cell Immunol.* 2019;345:103992.



High-risk Patients Are More Likely to Develop Influenza-related Complications*

Influenza-Related Complications¹

Moderate

- Sinus infection
- Ear infection

Severe

- Pneumonia
- **Worsening of chronic medical conditions**
- Myositis/rhabdomyolysis
- Multiorgan failure
- Sepsis
- **Myocarditis[†]**
- **Encephalitis[‡]**

Influenza can make chronic health problems worse (eg, COPD, diabetes, asthma, heart failure)^{1,4-7}

- **COPD:** Exacerbations and increased clinical visits (outpatient, ED, inpatient)
- **Diabetes:** Difficulty with blood glucose control⁵
- **Asthma:** Triggered attacks, worsening of symptoms, and potentially pneumonia⁶
- **Heart failure:** Increased in-hospital morbidity and mortality⁷

Most frequently described extrapulmonary complications⁸

Recognition of these complications is critical to initiating organ-specific supportive care

*Not all high-risk patients will develop influenza-related complications, but they are at a greater risk for complications than the general population¹⁻³; [†]viral myocarditis⁸; [‡]viral encephalitis.⁸

COPD=chronic obstructive pulmonary disease; ED=emergency department.

1. <https://www.cdc.gov/flu/symptoms/symptoms.htm>. Accessed February 5, 2020; 2. <https://www.cdc.gov/flu/about/disease/complications.htm>. Accessed January 30, 2020;

3. Mertz D et al. *BMJ*. 2013;347:f506; 4. Wallick C et al. Presented at Options X; August 28–September 1, 2019; Suntec, Singapore. 11163; 5. <https://www.cdc.gov/flu/highrisk/diabetes.htm>. Accessed January 30, 2020; 6. https://www.cdc.gov/asthma/asthma_stats/flu-vaccine-among-adults-with-current-asthma.html. Accessed January 30, 2020; 7. Panhwar MS et al. *JACC Heart Fail*. 2019;7:112-117;

8. Sellers SA et al. *Influenza Other Respir Viruses*. 2017;11:372-393.



Improvement of Influenza Symptoms

Seven (7) symptoms are typically associated with influenza¹

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Scoring System²

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In High-risk Patients

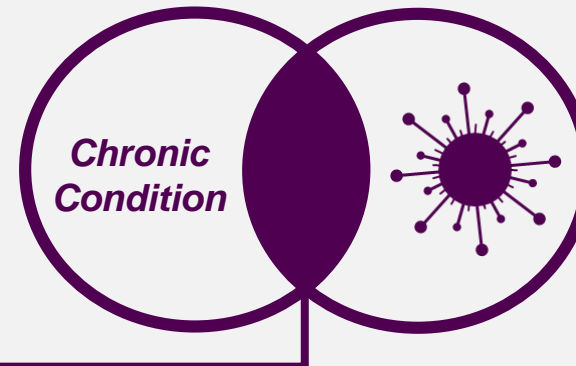


Underlying conditions, illness manifestations, and clinical outcomes vary widely⁵

In clinical trials, pre-existing conditions and symptoms at baseline are relevant considerations for evaluating the efficacy of antiviral treatment⁵

Symptoms of influenza can overlap with those of chronic medical conditions (eg, COPD, asthma)^{3,4}

- **Cough**
- **Nasal congestion**
- **Aches and pains**
- **Phlegm production**
- **Fatigue**
- **Shortness of breath**



COPD=chronic obstructive pulmonary disease.

1. <https://www.cdc.gov/flu/symptoms/symptoms.htm>. Accessed February 4, 2020; 2. Powers JH et al. *PLoS One*. 2018;13(3):e0194180; 3. Neuzil KM et al. *Clin Infect Dis*. 2003;36:169-174; 4. Asthma Symptoms | Cleveland Clinic. <https://my.clevelandclinic.org/health/articles/8953-asthma-symptoms>. Accessed February 6, 2020; 5. Ipson MG et al. *J Infect Dis*. 2010;201:1654-1662.

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