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# Using Antibiotic Wisely in the COVID-19 Era

Dr. Jerome Leis MD MSc
Dr. Philip Lam MD MSc

PHO Rounds
November 17, 2020

Sunnybrook
HEALTH SCIENCES CENTRE

# Faculty/Presenter Disclosure

Faculty: **Dr. Jerome Leis**

I have the following relevant financial relationships to disclose (past 2 years):

Relationships with financial sponsors:

- None

Relationships with commercial interests:

- None

Sunnybrook
ANTIMICROBIAL STEWARDSHIP TEAM

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Sunnybrook
ANTIMICROBIAL STEWARDSHIP TEAM

# By the end of this session, participants will be able to:

1. Identify tools and resources that can be used to improve the appropriateness of antibiotic prescribing for patients receiving virtual care

2. Describe the risk of bacterial co-infection in patients hospitalized with COVID-19 and explain opportunities to improve the quality of antibiotic use for these patients

3. List five factors associated with the COVID-19 pandemic that may impact antibiotic resistance at the population level globally

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# Case Presentation #1

- 68-year-old woman
  - History of hypertension, type 2 diabetes
  - 3-day history of mild dry cough and fever

- Virtual visit
  - Patient feels otherwise well and denies shortness of breath

# Questions that a clinician faces

*Should this patient be sent for a COVID-19 test?*

*Would you arrange for an in-person assessment/ physical exam at this time?*

*Should antibiotics be prescribed empirically to cover the possibility of pneumonia?*

# Case Presentation #1

- 68-year-old woman
  - PMHx: hypertension, type 2 diabetes
  - CC: 3-day history of mild dry cough and fever
- Virtual visit
  - Patient feels otherwise well and denies shortness of breath - **Likely Dx: viral bronchitis**
  - **Viral prescription sent (secure email; screenshot)**
  - **Patient advised to get a COVID-19 test**
  - **Follow-up if needed**

# Patient calls back later that week…

- COVID-19 result – negative
- Symptoms not improving – patient reports cough is now productive
- Patient expresses worry that feeling worse

# What would be the most appropriate next step?

a) Fax a Rx for antibiotics to the patient's pharmacy as she probably does have pneumonia

b) Advise the patient to rest, drink lots of fluids, take Tylenol and call back in a few days if not better

c) Arrange for an in-person assessment +/- investigations

# Case Presentation #1 – follow-up

- In person assessment booked (with appropriate PPE)
  - Coarse crackles at bases
  - Expiratory wheezes
  - CXR ordered - no evidence of pneumonia

- Diagnosis – Viral bronchitis
  - Prescribed bronchodilator, supportive therapy, advised to follow-up in 3 to 5 days if not improved

- A few days later – patient feels better, decides not to book follow-up

# *Using Antibiotics Wisely* – iteratively since 2017


https://choosingwiselycanada.org/campaign/antibiotics-primary-care

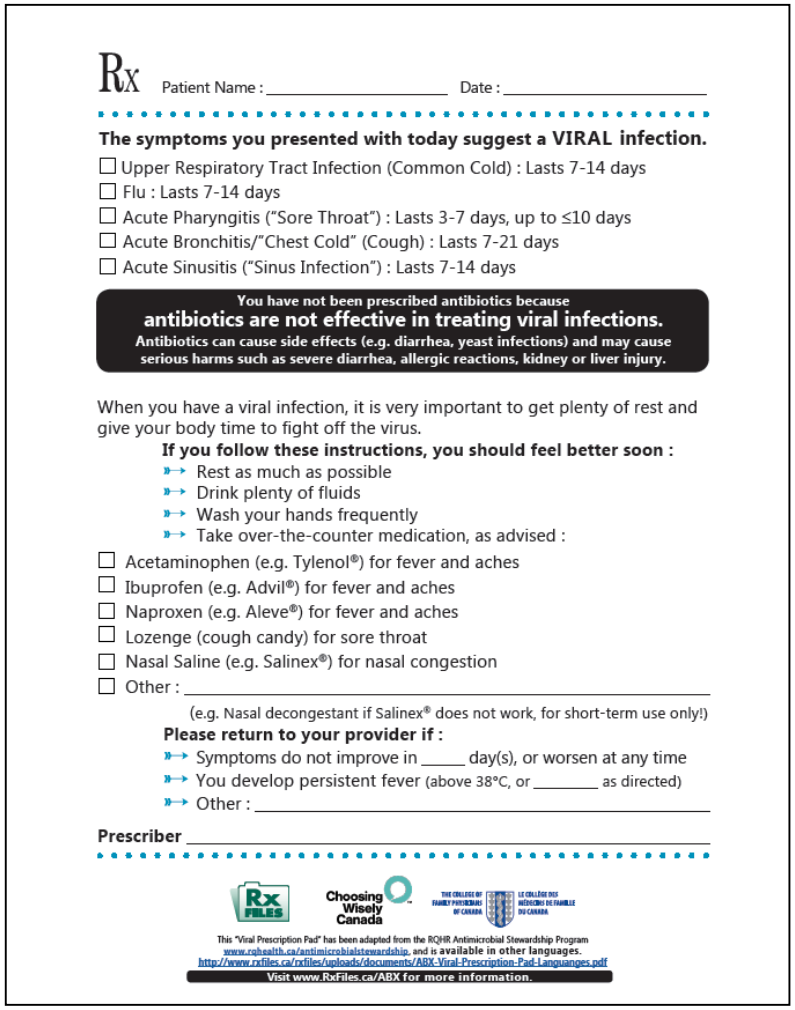
Public Health Agency of Canada
Agence de la santé publique du Canada

# Viral Prescription

- **Available languages:**
  - English, French (CWC)
  - Arabic, Chinese (Traditional and Simplified), Farsi (Persian), German, Hindi, Romanian, Russian, Spanish, Ukrainian, Urdu (Rx Files)

**Available via EMR**

**Satisfaction linked to reassurance, info, and symptom relief**



Rx Patient Name : _____ Date : _____

**The symptoms you presented with today suggest a VIRAL infection.**

- ☐ Upper Respiratory Tract Infection (Common Cold) : Lasts 7-14 days
- ☐ Flu : Lasts 7-14 days
- ☐ Acute Pharyngitis ("Sore Throat") : Lasts 3-7 days, up to ≤10 days
- ☐ Acute Bronchitis/"Chest Cold" (Cough) : Lasts 7-21 days
- ☐ Acute Sinusitis ("Sinus Infection") : Lasts 7-14 days

**You have not been prescribed antibiotics because**
**antibiotics are not effective in treating viral infections.**
**Antibiotics can cause side effects (e.g. diarrhea, yeast infections) and may cause serious harms such as severe diarrhea, allergic reactions, kidney or liver injury.**

When you have a viral infection, it is very important to get plenty of rest and give your body time to fight off the virus.

**If you follow these instructions, you should feel better soon :**

- ➳ Rest as much as possible
- ➳ Drink plenty of fluids
- ➳ Wash your hands frequently
- ➳ Take over-the-counter medication, as advised :

- ☐ Acetaminophen (e.g. Tylenol®) for fever and aches
- ☐ Ibuprofen (e.g. Advil®) for fever and aches
- ☐ Naproxen (e.g. Aleve®) for fever and aches
- ☐ Lozenge (cough candy) for sore throat
- ☐ Nasal Saline (e.g. Salinex®) for nasal congestion
- ☐ Other : _____

(e.g. Nasal decongestant if Salinex® does not work, for short-term use only!)

**Please return to your provider if :**

- ➳ Symptoms do not improve in _____ day(s), or worsen at any time
- ➳ You develop persistent fever (above 38°C, or _____ as directed)
- ➳ Other : _____

**Prescriber** _____

Rx FILES · Choosing Wisely Canada · The College of Family Physicians of Canada · Le Collège des médecins de famille du Canada

This "Viral Prescription Pad" has been adapted from the RQHR Antimicrobial Stewardship Program www.rqhealth.ca/antimicrobialstewardship, and is available in other languages. http://www.rxfiles.ca/rxfiles/uploads/documents/ABX-Viral-Prescription-Pad-Languages.pdf

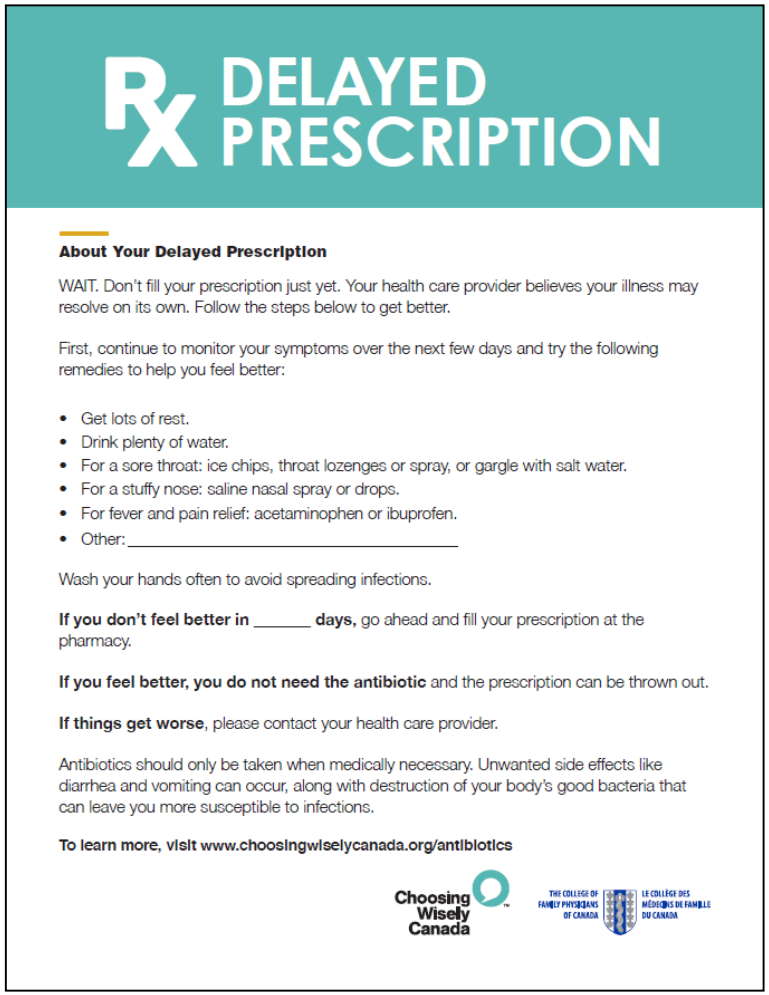
Visit www.RxFiles.ca/ABX for more information.

# Delayed Prescription

- **Available languages:**
  - English, French, Simplified Chinese, Spanish, Arabic, Punjabi and Tagalog

**Decreases antibiotic use**

**No difference in satisfaction**



## Rx DELAYED PRESCRIPTION

**About Your Delayed Prescription**

WAIT. Don't fill your prescription just yet. Your health care provider believes your illness may resolve on its own. Follow the steps below to get better.

First, continue to monitor your symptoms over the next few days and try the following remedies to help you feel better:

- Get lots of rest.
- Drink plenty of water.
- For a sore throat: ice chips, throat lozenges or spray, or gargle with salt water.
- For a stuffy nose: saline nasal spray or drops.
- For fever and pain relief: acetaminophen or ibuprofen.
- Other: _____

Wash your hands often to avoid spreading infections.

**If you don't feel better in _____ days,** go ahead and fill your prescription at the pharmacy.

**If you feel better, you do not need the antibiotic** and the prescription can be thrown out.

**If things get worse**, please contact your health care provider.

Antibiotics should only be taken when medically necessary. Unwanted side effects like diarrhea and vomiting can occur, along with destruction of your body's good bacteria that can leave you more susceptible to infections.

**To learn more, visit www.choosingwiselycanada.org/antibiotics**

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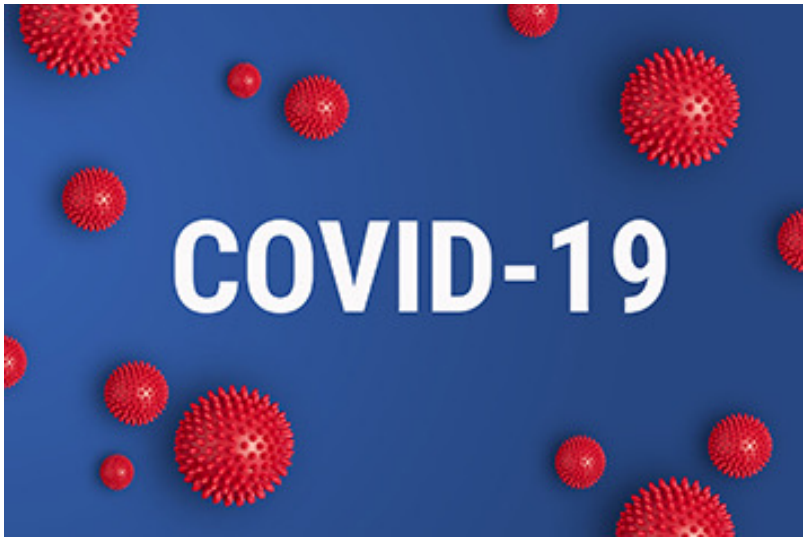
# Barriers in the Era of COVID-19…

- Shift to virtual care to reduce risk of in-office transmission
- Lack of PPE needed to assess symptomatic patients in person
- Concern that some jurisdictional COVID-19 'Assessment Centres' only offer testing, but no physical examination
- Persistent symptoms despite negative COVID-19 test result

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# How Should we Adapt Practice During the COVID-19 Pandemic?

- Best available evidence

- Stakeholder review
  - Choosing Wisely Canada Family Medicine Advisory Committee
  - 1-on-1 national stakeholder interviews by the Implementation Research Network
  - College of Family Physicians of Canada
  - Canadian Nurses Association
  - Public Health Agency of Canada

BMJ 2020
doi: https://doi.org/10.1136/bmj.m4125
(Published 13 November 2020)

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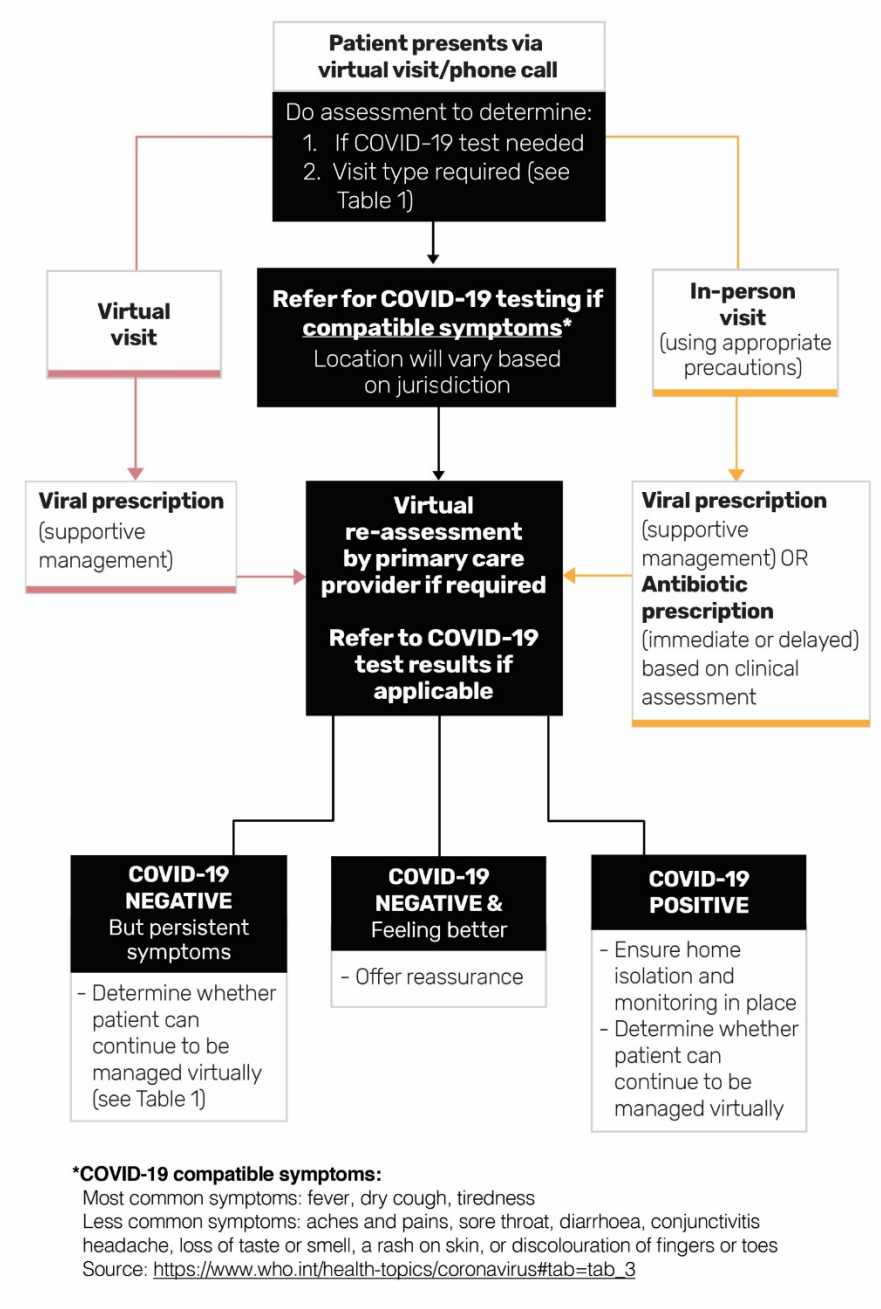
# The Cold Standard

## A Toolkit for Using Antibiotics Wisely in the Era of COVID-19 and Virtual Care

**SECOND EDITION | 2020**

# Managing RTIs: Virtual Care and COVID-19



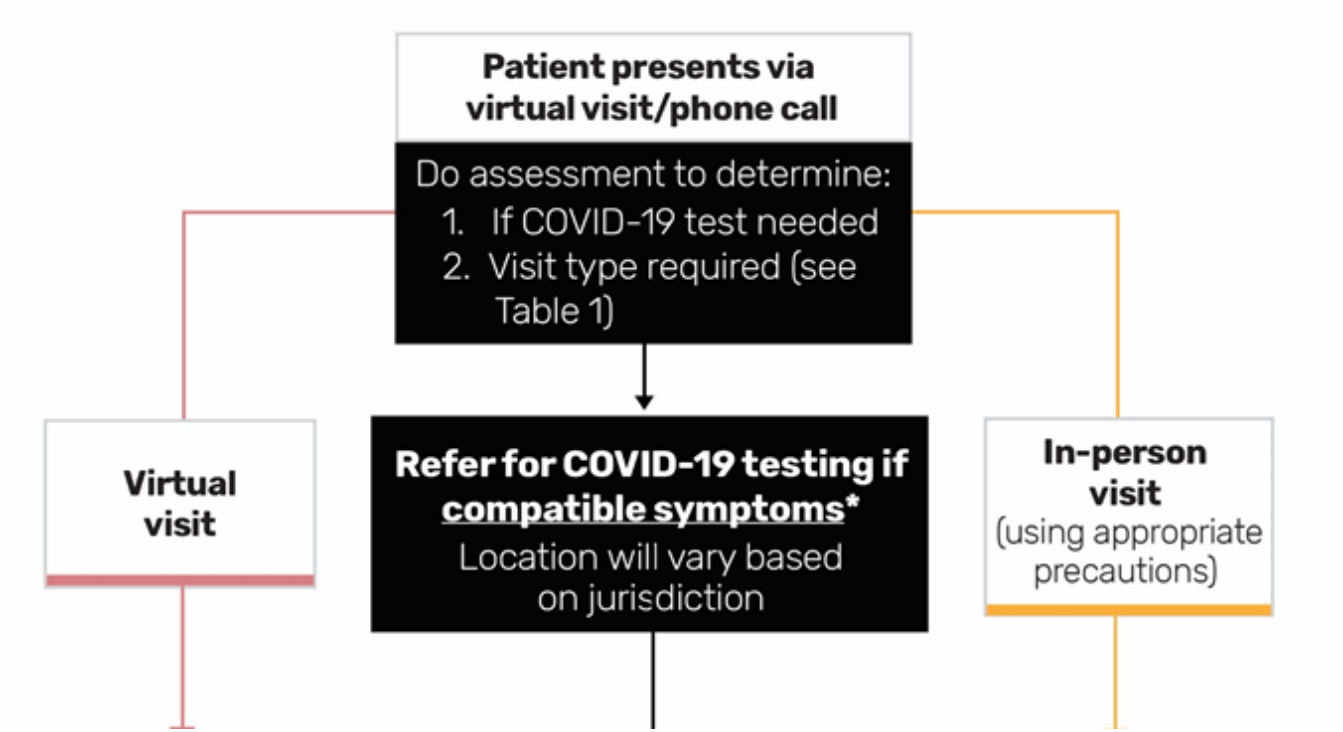
# It always starts with a virtual visit…

**2 immediate questions:**

- Does this person need a COVID test?
- Do they need to be examined in-person (e.g. alternate diagnosis; severity of symptoms)?

**Then:**

- Will they benefit from antibiotics (as opposed to a Viral Rx)?



# COVID-19 Compatible Symptoms

- New or worsening cough
- Shortness of breath or difficulty breathing
- Temperature equal to or over 38°C
- Feeling feverish
- Chills, fatigue or weakness
- Muscle or body aches
- New loss of smell or taste
- Headache
- Gastrointestinal symptoms (abdominal pain, diarrhea, vomiting)
- Feeling very unwell
- *Sore throat*
- *Runny nose*

Source: Health Canada

# Continue with Virtual Visit or Arrange for an In-Person Visit?

- Depends on your presumed diagnosis & severity of symptoms

| | INDICATIONS FOR VIRTUAL VISIT | INDICATIONS FOR IN-PERSON VISIT |
|---|---|---|
| **SUSPECTED OR CONFIRMED COVID-19** | • Fever<br>• Respiratory symptoms<br>• No shortness of breath | • Shortness of breath or hypoxia (if monitoring available)<br>• Concerns of dehydration<br>• Suspicion of secondary bacterial infection<br>• Any red flags** |
| **EAR PAIN** (In children over 6 months of age) | • Symptoms <48 hours<br>• Fever <39°C<br>• Pain controlled with oral pain medication<br>• Otherwise feels well | • Symptoms >48 hours despite adequate pain medications<br>• Fever ≥39°C<br>• Feels unwell |
| **SORE THROAT** | • Mild symptoms <48 hours<br>• Low suspicion for bacterial pharyngitis, e.g.:<br>  ○ Over 15 years of age<br>  ○ No fever<br>  ○ Presence of cough or runny nose | • Persistent or worsening symptoms >48 hours, or<br>• High suspicion of bacterial pharyngitis, e.g.:<br>  ○ Severe pain<br>  ○ No cough or runny nose<br>  ○ Fever without alternate cause |
| **SINUS CONGESTION** | • Mild symptoms <7 days<br>• No red flags*** | • Presence of red flags*** |
| **COPD EXACERBATION** | • Patient able to do their activities of daily living<br>• Patient known to provider and reliable for virtual follow-up | • Patient is too short of breath to do their activities of daily living |
| **SUSPECTED PNEUMONIA** | • Should be assessed in-person | • Assess clinically |
| **INFLUENZA-LIKE ILLNESS, BRONCHITIS, COMMON COLD, ASTHMA** | • High fever controllable with antipyretic<br>• Cough<br>• Congestion<br>• Body aches<br>• Mild GI symptoms | • Concerns of dehydration<br>• Suspicion of secondary bacterial infection<br>• Any red flags** |

# Suspected or Confirmed COVID-19

| |  INDICATIONS FOR VIRTUAL VISIT |  INDICATIONS FOR IN-PERSON VISIT |
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| **SUSPECTED OR CONFIRMED COVID-19** | • Fever<br>• Respiratory symptoms<br>• No shortness of breath | • Shortness of breath or hypoxia (if monitoring available)<br>• Concerns of dehydration<br>• Suspicion of secondary bacterial infection<br>• Any red flags** |

# Suspected or Confirmed COVID-19

**Red flags for children:**

- Fast or trouble breathing
- Bluish lips/face
- Intercostal indrawing
- Chest pain
- Refusing to walk
- Dehydration
- Seizure
- Fever if younger than 12 weeks

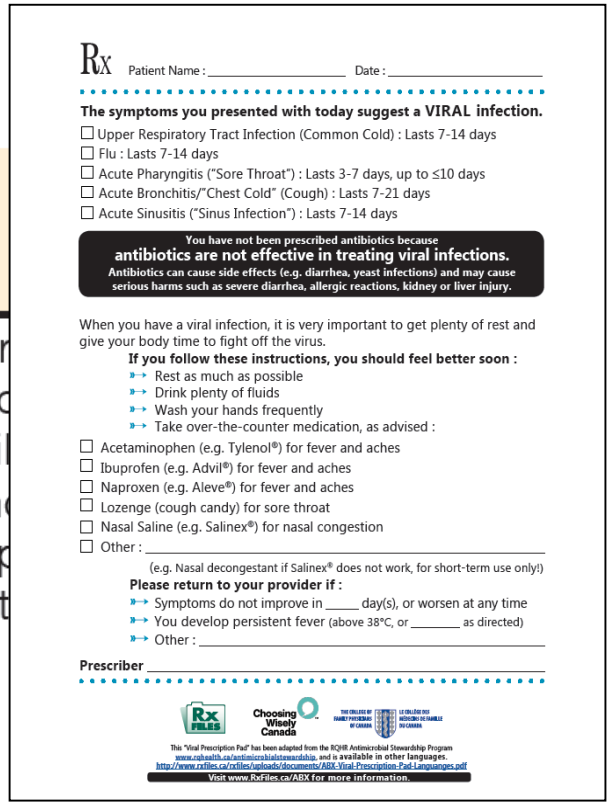
**Red flags for adults:**

- Shortness of breath
- Chest pain
- Abdominal pain
- Dizziness
- Confusion
- Dehydration

# Suspected or Confirmed COVID-19

There is no role for antibiotics to treat COVID-19 in the outpatient primary care setting

If RTI is deemed to be viral in nature, use a Viral Rx as part of your management plan



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When you have a viral infection, it is very important to get plenty of rest and give your body time to fight off the virus.

**If you follow these instructions, you should feel better soon :**

- ➳ Rest as much as possible
- ➳ Drink plenty of fluids
- ➳ Wash your hands frequently
- ➳ Take over-the-counter medication, as advised :

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(e.g. Nasal decongestant if Salinex® does not work, for short-term use only!)

**Please return to your provider if :**

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**Prescriber** _____

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This "Viral Prescription Pad" has been adapted from the RCHR Antimicrobial Stewardship Program www.rqhealth.ca/antimicrobialstewardship, and is available in other languages. http://www.rxfiles.ca/rxfiles/uploads/documents/ABX-Viral-Prescription-Pad-Languages.pdf

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# Ear Pain

| | INDICATIONS FOR VIRTUAL VISIT | INDICATIONS FOR IN-PERSON VISIT |
|---|---|---|
| **EAR PAIN** (In children over 6 months of age) | • Symptoms <48 hours<br>• Fever <39°C<br>• Pain controlled with oral pain medication<br>• Otherwise feels well | • Symptoms >48 hours despite adequate pain medications<br>• Fever ≥39°C<br>• Feels unwell |

# Sore Throat

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# Sore Throat

**During an in-person visit, antibiotics should only be prescribed if:**

- Patient has a moderate to high likelihood of having Group A Strep based on a validated predictive score (e.g. Modified Centor);

**AND**

- Patient has a positive throat culture/rapid Group A Strep test result

# Sinus Congestion

| |  INDICATIONS FOR VIRTUAL VISIT |  INDICATIONS FOR IN-PERSON VISIT |
|---|---|---|
| **SINUS CONGESTION** | • Mild symptoms <7 days<br>• No red flags*** | • Presence of red flags*** |

# Sinus Congestion

**Red Flags**:

- Altered mental status
- Severe Headache
- Systemic toxicity
- Orbital swelling
- Change in visual acuity
- Neurologic deficits

NDICATIONS FOR
N-PERSON VISIT

**SINUS CONGESTION**

- M
- N

ence of red flags***

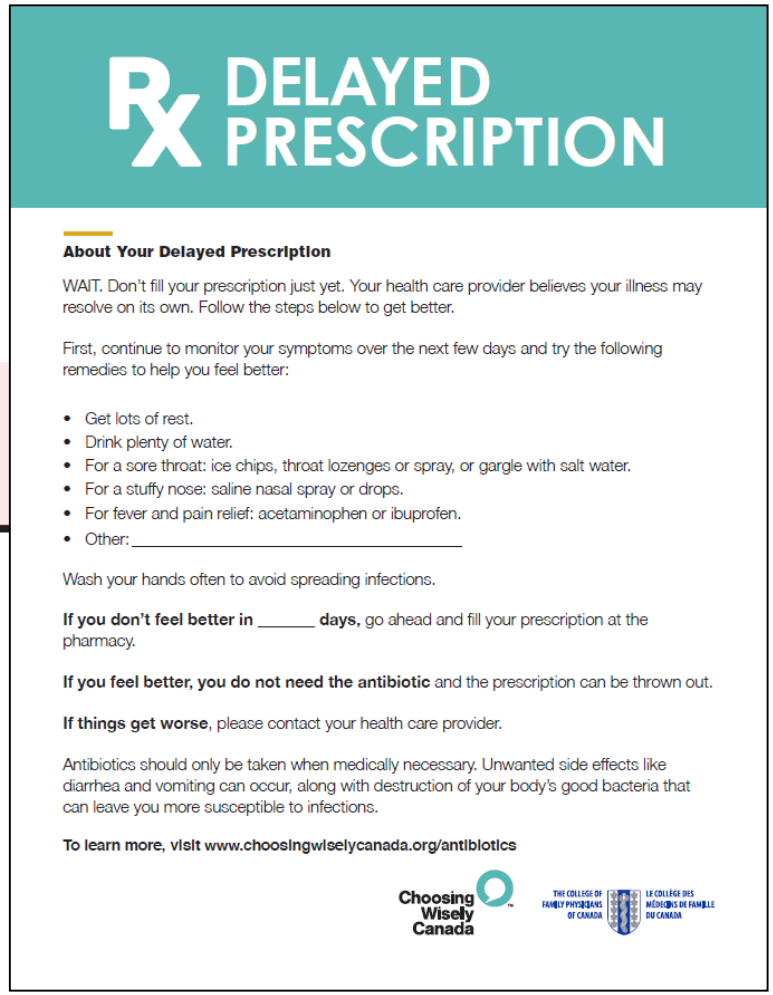
# Sinus Congestion

**Delayed Prescription:**

- Can be used during initial virtual visit if symptoms > 7 days;

**AND**

- No improvement following a 72 hour trial of nasal corticosteroids



## Rx DELAYED PRESCRIPTION

**About Your Delayed Prescription**

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- For a stuffy nose: saline nasal spray or drops.
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- Other: _____

Wash your hands often to avoid spreading infections.

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# COPD

| | INDICATIONS FOR VIRTUAL VISIT | INDICATIONS FOR IN-PERSON VISIT |
|---|---|---|
| **COPD EXACERBATION** | • Patient able to do their activities of daily living<br>• Patient known to provider and reliable for virtual follow-up | • Patient is too short of breath to do their activities of daily living |

# COPD

**During an in-person visit, antibiotics should only be prescribed if:**

- Patient has an increase in sputum purulence;

**AND**

- Patient has an increase in sputum volume AND/OR increased dyspnea

# Pneumonia

| | INDICATIONS FOR VIRTUAL VISIT | INDICATIONS FOR IN-PERSON VISIT |
|---|---|---|
| **SUSPECTED PNEUMONIA** | • Should be assessed in-person | • Assess clinically |

# Pneumonia

**During an in-person visit:**

- Patients with normal vital signs and no abnormal findings on respiratory exam are unlikely to have pneumonia and DO NOT need a CXR

- If CXR is indicated and signs consistent with pneumonia are reported, treat with antibiotics

# Influenza-Like Illness, Bronchitis, Common Cold, Asthma

| |  INDICATIONS FOR VIRTUAL VISIT |  INDICATIONS FOR IN-PERSON VISIT |
|---|---|---|
| **INFLUENZA-LIKE ILLNESS, BRONCHITIS, COMMON COLD, ASTHMA** | • High fever controllable with antipyretic<br>• Cough<br>• Congestion<br>• Body aches<br>• Mild GI symptoms | • Concerns of dehydration<br>• Suspicion of secondary bacterial infection<br>• Any red flags** |

# Influenza-Like Illness, Bronchitis, Common Cold, Asthma

**There is no role for antibiotics to treat these viral conditions**

**BRONCHITIS, COMMON COLD, ASTHMA**

- Congestion
- Body aches
- Mild GI symptoms

- bacterial infection
- Any red flags**

# Re-assess Virtually PRN

**Viral prescription**
(supportive management)

**Virtual re-assessment by primary care provider if required**

**Refer to COVID-19 test results if applicable**

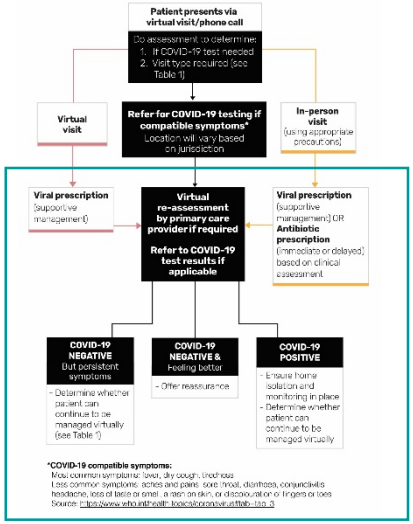
**Viral prescription**
(supportive management) OR **Antibiotic prescription**
(immediate or delayed) based on clinical assessment

**COVID-19 NEGATIVE**
But persistent symptoms
- Determine whether patient can continue to be managed virtually (see Table 1)

**COVID-19 NEGATIVE &**
Feeling better
- Offer reassurance

**COVID-19 POSITIVE**
- Ensure home isolation and monitoring in place
- Determine whether patient can continue to be managed virtually

***COVID-19 compatible symptoms:**
Most common symptoms: fever, dry cough, tiredness
Less common symptoms: aches and pains, sore throat, diarrhoea, conjunctivitis headache, loss of taste or smell, a rash on skin, or discolouration of fingers or toes
Source: https://www.who.int/health-topics/coronavirus#tab=tab_3



# Summary:
# RTI in primary care during the pandemic

**2 immediate questions:**

- Does this person need a COVID test?
- Do they need to be examined in-person (e.g. alternate diagnosis; severity of symptoms)?

**Then:**

- Will they benefit from antibiotics (as opposed to a Viral Rx)?

# Case #2

- 68 year-old woman with history of diabetes, hypertension presents with a 3-day history of cough, myalgia, fever and increasing confusion
- Found to be hypoxemic (88% saturation on room air) → improves to 95% on 2 litres of supplemental oxygen by nasal prongs
- Febrile (T 38.5 C) but hemodynamically stable

- Admitted to hospital for further management

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# Case #2: Continued

- Bloodwork shows: Hgb 112 WBC 5.6 (lymph 0.3) PLT 115 Cr 102
- Chest x-ray showed bilateral patchy ground-glass opacities
- Blood cultures are drawn, mid-turbinate swab obtained for COVID-19 testing
- Given intravenous fluids,1 gram IV ceftriaxone and 500 mg IV azithromycin in the Emergency Department

# Case #2: Continued

- Post-admission day 1: the patient's mid-turbinate swab has returned positive for **COVID-19**. The patient's clinical status is unchanged and blood cultures remain negative at 24 hours incubation. What will you do with regards to antibiotic therapy?

a) Continue IV ceftriaxone alone
b) Continue IV ceftriaxone and PO azithromycin
c) Transition to PO amoxicillin-clavulanate
d) Stop antibiotics and monitor

# COVID-19 Infection and Antibiotics

## Early in the pandemic:

Limited understanding of the infection

No therapeutic options available

Significant morbidity and mortality

Extrapolation of co-infection risk from influenza

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# COVID-19 Infection and Antibiotics

Early in the pandemic:

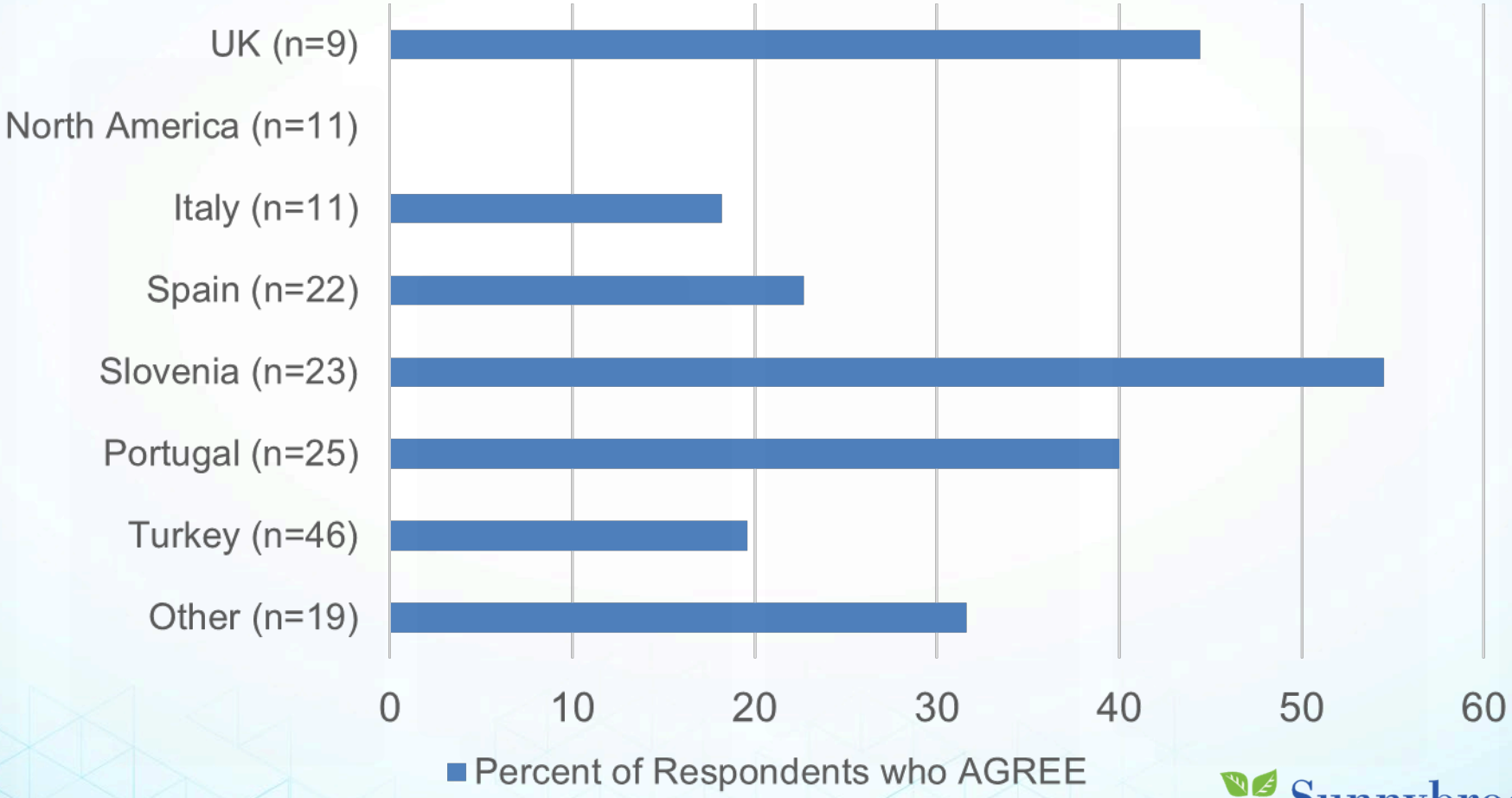
- Beović et al
  - International web-based survey investigating patterns of antibiotic use as reported by physicians
  - April 7 – 28, 2020
  - 166 participants from 23 countries and 82 different hospitals
  - Infectious diseases (50.3%), intensive care (28.5%) and internal medicine (11.5%)

Sunnybrook HEALTH SCIENCES CENTRE

Beovic et al. J Antimicrob Chemother. 2020 Nov 1;75(11):3386-3390.

# COVID-19 Infection and Antibiotics

*"We do not routinely prescribe antibiotics to the patients in the ward"*

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Beovic et al. J Antimicrob Chemother. 2020 Nov 1;75(11):3386-3390.

# COVID-19 Infection and Antibiotics

1. **Bacterial co-infection is relatively infrequent (< 10%) in hospitalised patients with COVID-19**
2. Persistent fevers are commonly seen in hospitalised patients with COVID-19 and does not necessarily indicate the presence of bacterial co-infection
3. Antibiotic use in patients with COVID-19 has not been proven to improve outcomes
4. Inappropriate use may reduce antibiotic availability, lead to *C. difficile* infection and increased antimicrobial resistance

Systematic Review

# Bacterial co-infection and secondary infection in patients with COVID-19: a living rapid review and meta-analysis

Bradley J. Langford [1,2,*], Miranda So [3,4,5], Sumit Raybardhan [6], Valerie Leung [1,7], Duncan Westwood [8], Derek R. MacFadden [9], Jean-Paul R. Soucy [10], Nick Daneman [1,4,8,11]

CMI CLINICAL MICROBIOLOGY AND INFECTION
ESCMID

- Meta-analysis of 24 cohort studies (N = 3338 hospitalised patients)

| | Estimate (%) | 95% CI |
|---|---|---|
| Bacterial co-infection at presentation | 3.5 | 0.4 – 6.7 |
| Secondary infection after presentation | 14.3 | 9.6 – 18.9 |
| Overall proportion with bacterial infection | 6.9 | 4.3 – 9.5 |

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Langford BJ et al. Clin Microbiol Infect. 2020 Jul 22;S1198-743X(20)30423-7.

https://www.tarrn.org/covid

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# Bacterial Co-Infection and Secondary Infection in Patients with COVID-19: A Rapid Systematic Review and Meta-Analysis

Importance:

Bacterial pathogens are commonly identified in viral respiratory infections such as influenza and are an important cause of morbidity and mortality. The prevalence of bacterial infection in patients infected with SARS-CoV-2 is not well understood.

Objective:

To determine the prevalence of bacterial co-infection (at presentation) and secondary infection (after presentation) in patients with COVID-19.

Overall Percent with Bacterial Infection (%): **8.0 (6.1, 9.9)**

**4.9** (2.6 to 7.1)
Co-infection (%)

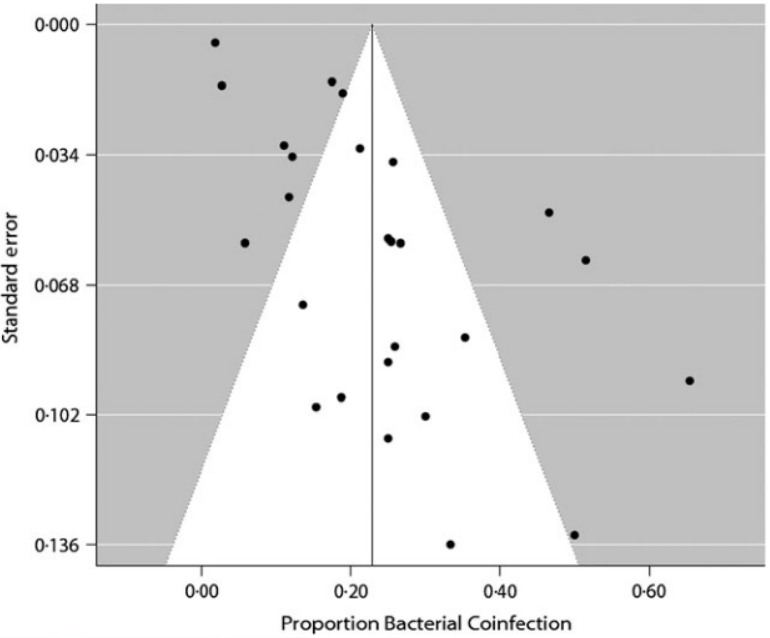
**16.0** (12.4 to 19.6)
Secondary Infection (%)

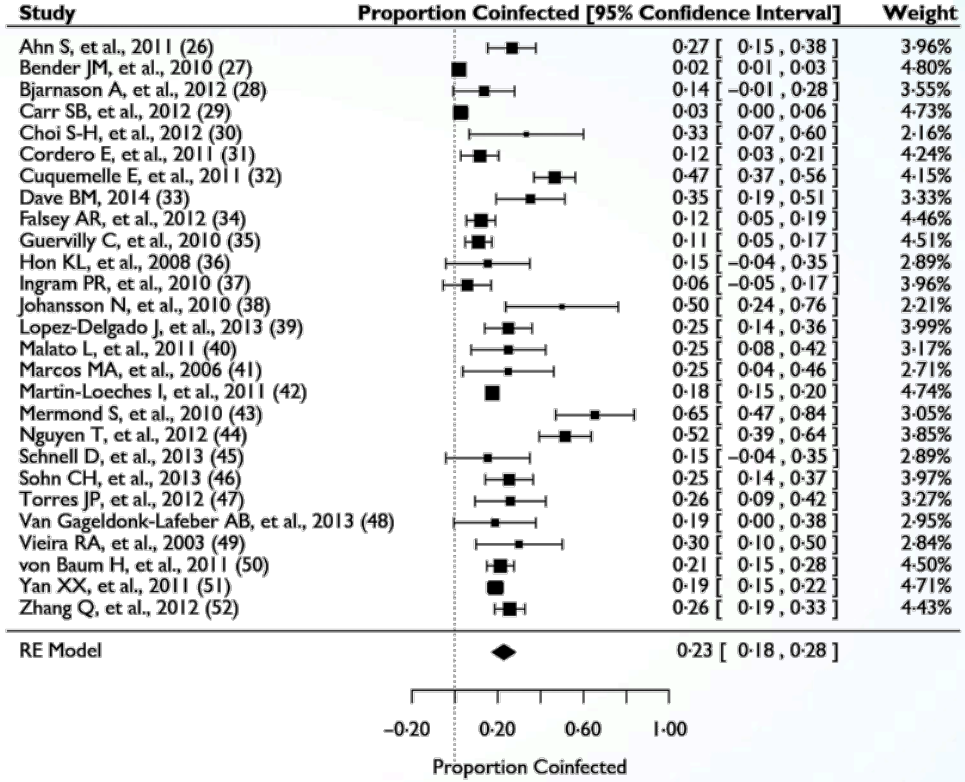
**5.9** (4.4 to 7.4)
All Patients (%)

**16.0** (11.6 to 20.4)
Critically Ill (%)

# The frequency of influenza and bacterial coinfection: a systematic review and meta-analysis

Eili Y. Klein,[a,b] Bradley Monteforte,[c] Alisha Gupta,[d] Wendi Jiang,[b] Larissa May,[e] Yu-Hsiang Hsieh,[a] Andrea Dugas[a]




**Estimated rate of bacterial co-infection with influenza: 23%**

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Klein EY et al. Influenza Other Respir Viruses. 2016 Sep;10(5):394-403.

# The role of pneumonia and secondary bacterial infection in fatal and serious outcomes of pandemic influenza a(H1N1)pdm09

Chandini Raina MacIntyre[1], Abrar Ahmad Chughtai[2*], Michelle Barnes[2], Iman Ridda[2], Holly Seale[2], Renin Toms[2] and Anita Heywood[2]

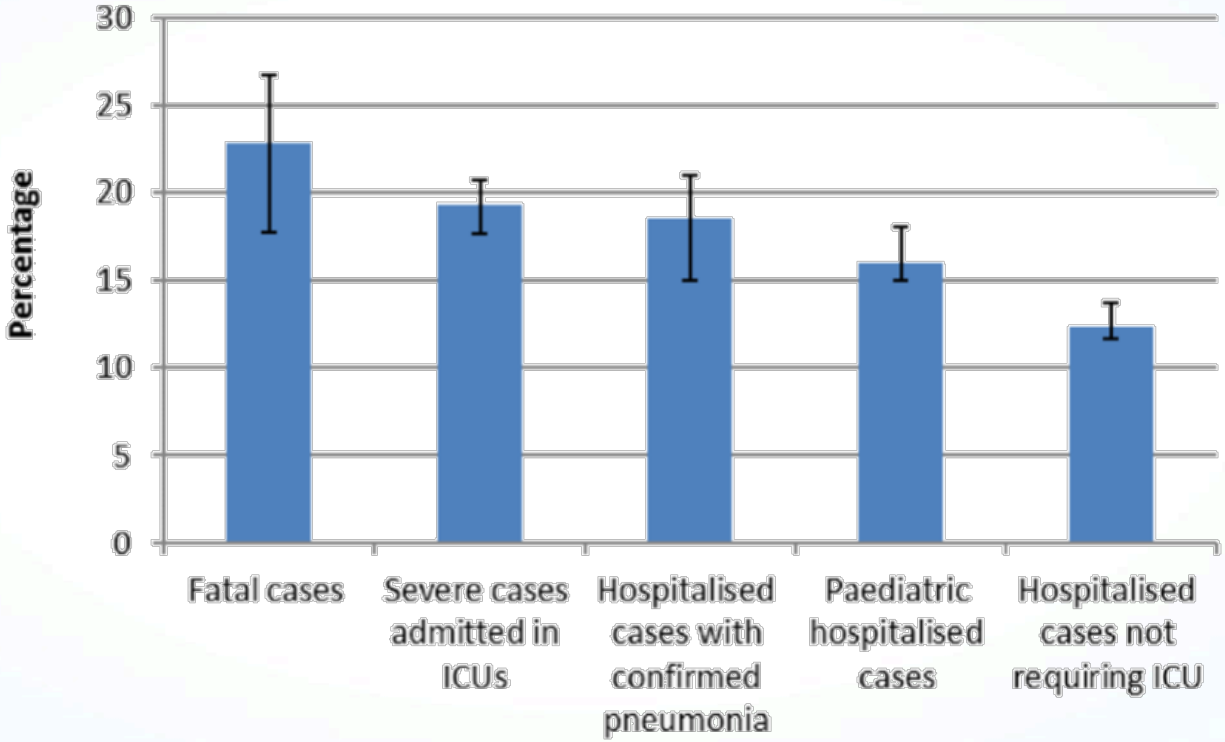


**Fig. 2** Average prevalence of bacterial infection in fatal, ICU admitted, general ward admitted and paediatric patients

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MacIntyre CR et al. BMC Infect Dis. 2018 Dec 7;18(1):637.

# COVID-19 Infection and Antibiotics

1. Bacterial co-infection is relatively infrequent (< 10%) in hospitalised patients with COVID-19
2. **Persistent fevers are commonly seen in hospitalised patients with COVID-19 and does not necessarily indicate the presence of bacterial co-infection**
3. Antibiotic use in patients with COVID-19 has not been proven to improve outcomes
4. Inappropriate use may reduce antibiotic availability, lead to *C. difficile* infection and increased antimicrobial resistance

# COVID-19 Duration of Fever

| Study | Population | Duration of Fever |
|---|---|---|
| Chen J<br>(J Infection 2020) | 249 hospitalised patients<br>87.1% with fever<br>Median age = 51 years | 10 days (95% CI 8 – 11) |
| Zhou F<br>(Lancet 2020) | 191 hospitalised patients<br>94% with fever (T >37.3)<br>Median age = 56 years | 12 days (95% CI 8 – 13) |
| Han J<br>(Epidemiol Infect 2020) | 182 hospitalised patients<br>74.6% with fever<br>Median age = 44 years | Severe disease (N=27): 7 days<br>Mild disease (N= 155): 2 days |

**Persistent fevers are commonly seen in hospitalised patients with COVID-19 infection**

Chen J et al. J Infect. 2020 May; 80(5): e1–e6.
Zhou F et al. Lancet. 2020 Mar 28;395(10229):1054-1062.
Han J et al. Epidemiol Infect. 2020; 148: e125.

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# GI Symptoms in COVID-19 Infection

- Up to 20% of patients with low-severity disease will have diarrhea as presenting symptom
- Approximately 20% of hospitalised patients receiving antibiotic will develop an adverse drug event (GI symptoms being most common)
- Concomitant antibiotic use may exacerbate GI symptoms related to COVID-19 and increase the risk of *C. difficile* infection

Chaoqun H et al. Am J Gastroenterol. 2020 Jun;115(6):916-923.
Tamma PD et al. JAMA Intern Med. 2017 Sep 1; 177(9):1308-1315

# GI Symptoms in COVID-19 Infection

**_Clostridiodes difficile_ in COVID-19 Patients, Detroit, Michigan, USA, March–April 2020**

Avnish Sandhu, Glenn Tillotson, Jordan Polistico, Hossein Salimnia, Mara Cranis, Judy Moshos, Lori Cullen, Lavina Jabbo, Lawrence Diebel, Teena Chopra

- March – April 2020: 9 patients with severe COVID-19 who developed *C. difficile* infection
- 3 patients received antibiotics before admission, 8 patients received antibiotics at the time of admission
- Four patients died during hospitalization

Increase in CDI rate from 3.32/10,000 PDs → 3.6/10,000 PDs

Sandhu A et al. Emerg Infect Dis. 2020 Sep; 26(9): 2299–2300.

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# What do the guidelines recommend?

SUMMARY

# Ontario COVID-19 Clinical Practice Guidelines
# Antimicrobial and Immunomodulatory Therapy in Adult Patients with COVID-19

**Recommendations in this document apply to patients >18 years of age. For recommendations in special populations, refer to the complete guidelines.** Last updated on October 22, 2020

There is emerging evidence to guide antiviral management for ill patients with COVID-19.

The guidelines recommend that infectious diseases consultation (where available) be obtained before any investigational treatment is offered to a patient with COVID-19 outside of a clinical trial, and that informed consent be obtained from the patient or substitute decision-maker.

| SEVERITY OF ILLNESS | ANTIVIRAL | IMMUNOMODULATORY | ANTIBACTERIAL |
|---|---|---|---|
| **Critically Ill Patients**<br>**Hospitalized, ICU-based**<br>Patients requiring ventilatory and/or circulatory support; also includes patients requiring high-flow nasal cannula, non-invasive ventilation, or higher concentrations of oxygen by mask | ▸ **Remdesivir**: It is **not recommended** to initiate remdesivir for patients on ECMO or receiving mechanical ventilation outside of a clinical trial. **No recommendation can be made** on the initiation of remdesivir in those on high-flow nasal cannula, non-invasive ventilation, or higher concentrations of oxygen by mask. (Reason: lack of consensus)<br>▸ **Chloroquine** or **hydroxychloroquine** is **not** recommended for treatment of COVID-19<br>▸ **Lopinavir/ritonavir** is **not** recommended for treatment of COVID-19 | ▸ **Dexamethasone** 6 mg PO/IV daily x 10 days (or until discharge if sooner) is **recommended** for critically ill patients<br>▸ **Tocilizumab** (IL-6 inhibitor) should **not** be offered routinely outside of clinical trials; may be considered on an individual basis in patients with cytokine storm (with expert consultation)<br>▸ **COVID-19 convalescent plasma** is currently **unavailable** in Canada in critically ill patients and is unavailable outside of clinical trials<br>▸ **Interferon** (with or without combination of lopinavir-ritonavir and ribavirin) is **not** recommended outside of clinical trials | ▸ **Ceftriaxone** 1 g IV q24h x 5 days is recommended if there is concern for bacterial co-infection (Alternative for severe beta-lactam hypersensitivity: levofloxacin 750 mg IV or moxifloxacin 400 mg IV q24h x 5 days)<br>▸ Add azithromycin 500 mg IV q24h x 5 days to ceftriaxone empiric therapy if *Legionella* infection is suspected (azithromycin is not needed if empiric therapy is levofloxacin or moxifloxacin)<br>▸ De-escalate on the basis of microbiology results and clinical judgment |
| **Moderately Ill Patients**<br>**Hospitalized, ward-based**<br>Patients requiring low-flow supplemental oxygen | ▸ **Remdesivir** 200 mg IV loading on Day 1, then 100 mg IV daily x 4 days or until discharge (whichever comes first) **can be considered** for **moderately ill** patients. **Preference should be given to** enrolling in eligible clinical trials evaluating remdesivir. | ▸ **Dexamethasone** 6 mg PO/IV daily x 10 days (or until discharge if sooner) is **recommended** for **moderately ill** patients | ▸ Antibacterial therapy is **not** routinely recommended outside of clinical trials or where other indications would justify its use |
| **Mildly Ill Patients**<br>**Ambulatory, outpatient**<br>Patients who do not require supplemental oxygen, intravenous fluids, or other physiological support | ▸ **Chloroquine** or **hydroxychloroquine** (with or without azithromycin) is **not** recommended for treatment of COVID-19<br>▸ **Lopinavir/ritonavir** is **not** recommended for treatment of COVID-19<br>▸ **Remdesivir** is **not** recommended for **mildly ill** patients outside of a clinical trial. | ▸ **Tocilizumab** is **not** recommended outside of clinical trials<br>▸ **COVID-19 convalescent plasma** is **not** recommended outside of clinical trials *(unavailable outside of clinical trials)*<br>▸ **Interferon** (with or without combination of lopinavir-ritonavir and ribavirin) is **not** recommended outside of clinical trials<br>▸ **Dexamethasone** is **not** recommended for **mildly ill** patients | Click here for dosing and pharmacologic considerations for medications under investigation |

▸ Numerous therapies (e.g. vitamin C, ivermectin) have shown a theoretical or mechanistic basis to be beneficial in the management against COVID-19, however clinical data for these therapies are lacking. Refer to the guidelines for further discussion.
▸ Recommendations in this document are based on best available data and may change as additional data become available. The complete and most up-to-date version of the guidelines is available at www.antimicrobialstewardship.com/covid-19.

**https://www.antimicrobialstewardship.com/covid-19**

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Ontario COVID-19 Clinical Practice Guidelines

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| SEVERITY OF ILLNESS | ANTIVIRAL | IMMUNOMODULATORY | ANTIBACTERIAL |
|---|---|---|---|

## In Moderately Ill Patients

(hospitalised, ward-based, requiring low-flow supplemental oxygen):

Antibacterial therapy is **not** routinely recommended outside of clinical trials or where other indications would justify its use.

- **Chloroquine** or **hydroxychloroquine** (with or without azithromycin) is **not** recommended for treatment of COVID-19
- **Lopinavir/ritonavir** is **not** recommended for treatment of COVID-19
- **Remdesivir** is **not** recommended for **mildly ill** patients outside of a clinical trial.
- **Tocilizumab** is **not** recommended outside of clinical trials
- **COVID-19 convalescent plasma** is **not** recommended outside of clinical trials *(unavailable outside of clinical trials)*
- **Interferon** (with or without combination of lopinavir-ritonavir and ribavirin) is **not** recommended outside of clinical trials
- **Dexamethasone** is **not** recommended for **mildly ill** patients

Click here for dosing and pharmacologic considerations for medications under investigation

### Mildly Ill Patients

**Ambulatory, outpatient**

Patients who do not require supplemental oxygen, intravenous fluids, or other physiological support

- Numerous therapies (e.g. vitamin C, ivermectin) have shown a theoretical or mechanistic basis to be beneficial in the management against COVID-19, however clinical data for these therapies are lacking. Refer to the guidelines for further discussion.
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There is emerging evidence to guide antiviral management for ill patients with COVID-19.

The guidelines recommend that infectious diseases consultation (where available) be obtained before any investigational treatment is offered to a patient with COVID-19 outside of a clinical trial, and that informed consent be obtained from the patient or substitute decision-maker.

## Critically Ill Patients

(ICU-based patients requiring ventilatory and/or circulatory support):

Ceftriaxone 1 g IV q24h x 5 days if there is concern for bacterial co-infection

Add azithromycin 500 mg IV q24h x 5 days if *Legionella* infection is suspected

Patients who do not require supplemental oxygen, intravenous fluids, or other physiological support

**Remdesivir** is **not** recommended for **mildly ill** patients outside of a clinical trial.

**Dexamethasone** is **not** recommended for **mildly ill** patients

pharmacologic considerations for medications under investigation

- Numerous therapies (e.g. vitamin C, ivermectin) have shown a theoretical or mechanistic basis to be beneficial in the management against COVID-19, however clinical data for these therapies are lacking. Refer to the guidelines for further discussion.
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# Other Guidelines

| Guideline | Recommendation |
|---|---|
| Canadian Pediatric Society (April 2020) | *"Antibiotics are not recommended to treat cases of COVID-19 without clinical suspicion of bacterial co-infection."* |
| World Health Organization (May 2020) | *"For suspected or confirmed mild COVID-19, against the use of antibiotic therapy or prophylaxis. For suspected or confirmed moderate COVID-19, that antibiotics should not be prescribed unless there is clinical suspicion of a bacterial infection."* |
| Surviving Sepsis Campaign (June 2020) | *"In mechanically ventilated patients with COVID-19 and respiratory failure, we suggest using empiric antimicrobials/antibacterial agents, over no antimicrobials."* |
| National Institute for Health and Care Excellence (Oct 2020) | *"If there is confidence that the clinical features are typical for COVID-19, it is reasonable not to start empirical antibiotics."*<br><br>*"Empirical antibiotics should be started if there is clinical suspicion of bacterial infection, including characteristic symptoms and localised chest findings."* |

World Health Organization. (2020). Clinical management of COVID-19: interim guidance, 27 May 2020. World Health Organization. https://apps.who.int/iris/handle/10665/332196.
Canadian Pediatric Society. (2020). The acute management of pediatric coronavirus disease 2019 (COVID-19). https://www.cps.ca/en/documents/position/the-acute-management-of-paediatric-coronavirus-disease-2019covid-19.
Alhazzani W et al. Crit Care Med. 2020 Jun;48(6):e440-e469.
National Institute for Health and Care Excellence. (2020). COVID-19 rapid guideline: antibiotics for pneumonia in adults in hospital. https://www.nice.org.uk/guidance/ng173/chapter/3-Initial-approach-to-antibiotic-treatment-choices

# Case 2

- Post-admission day 1: the patient's mid-turbinate swab has returned positive for COVID-19. The patient's clinical status is unchanged and blood cultures remain negative at 24 hours incubation. What will you do with regards to the antibiotics?

a) Continue IV ceftriaxone alone

b) Continue IV ceftriaxone and PO azithromycin

c) Transition to PO amoxicillin-clavulanate

**d) Stop antibiotics and monitor**

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# COVID-19 and Antibiotic Resistance

Empiric antibiotic therapies associated with virtual care

Disruptions in the chronic disease management

Empiric antibiotic therapies in hospitalised patients with COVID-19

Hospital-acquired infections

Public Health and
Infection Prevention & Control

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# You should now be able to:

1. Identify tools and resources that can be used to improve the appropriateness of antibiotic prescribing for patients receiving virtual care

2. Describe the risk of bacterial co-infection in patients hospitalized with COVID-19 and explain opportunities to improve the quality of antibiotic use for these patients

3. List five factors associated with the COVID-19 pandemic that may impact antibiotic resistance at the population level globally

# Questions?

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