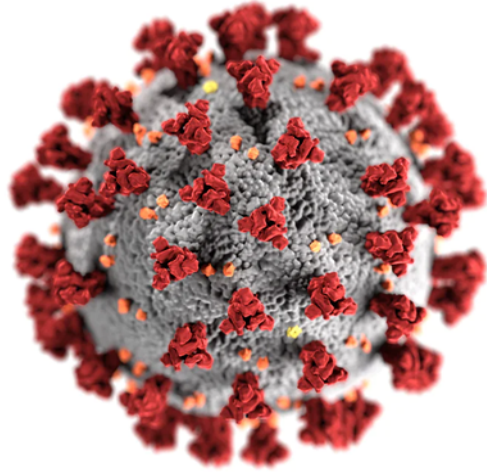


Clinical Management of COVID-19 Infections



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McGill Annual Refresher Course for Family Physicians,
December 1, 2020

Disclosures

- No conflicts of interest
- Have received investigator initiated research grants from AbbVie, GSK
- Have been the PI on pharmaceutical trials for Merck and Sanofi Pasteur

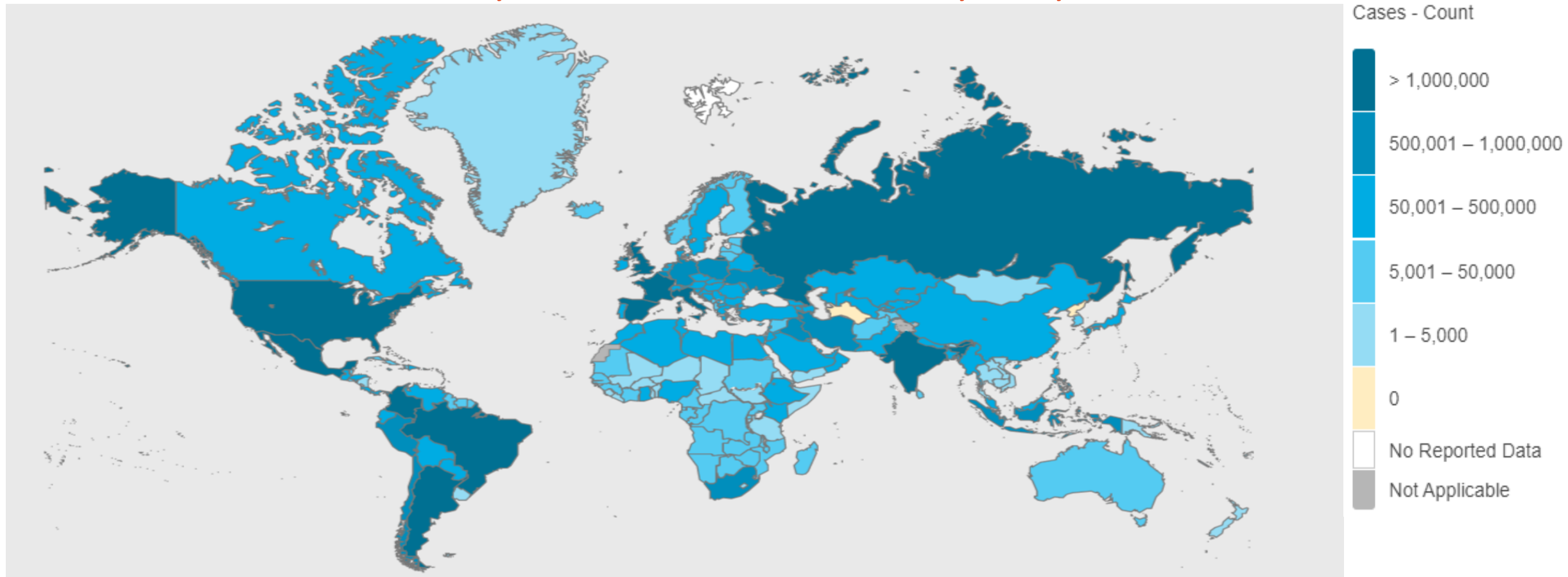
Learning Objectives

- Review the epidemiology and risk of transmission of SARS-CoV-2
- Become familiar with the different clinical presentations and clinical course of COVID-19 across the spectrum of disease
- Understand the different diagnostic tests used for SARS-CoV-2 and their limitations
- Be aware of the different therapeutic and management options for COVID-19 across the spectrum of disease



Global COVID-19 Cases as of Nov 24, 2020

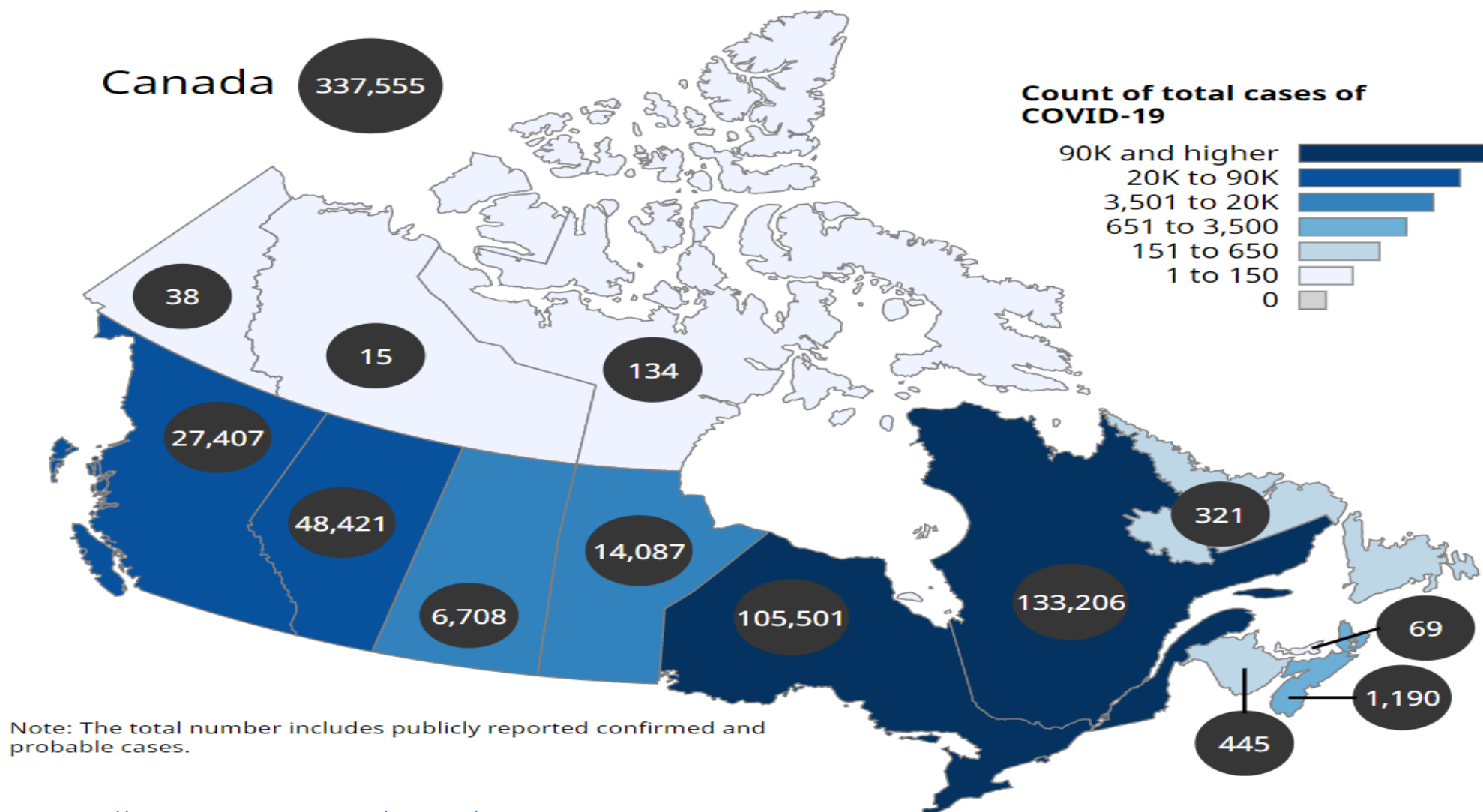
Cases: **59,939,306** Deaths: **1,412,669**



1. WHO. 2020. <https://covid19.who.int/>. WHO Coronavirus Disease (COVID-19) Dashboard. Updated 2020/11/24

2. JHU. 2020. <https://www.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6>. COVID-19 Dashboard by the CSSE at JHU. Updated 2020/11/25

COVID-19 Cases Canada as of Nov 23, 2020

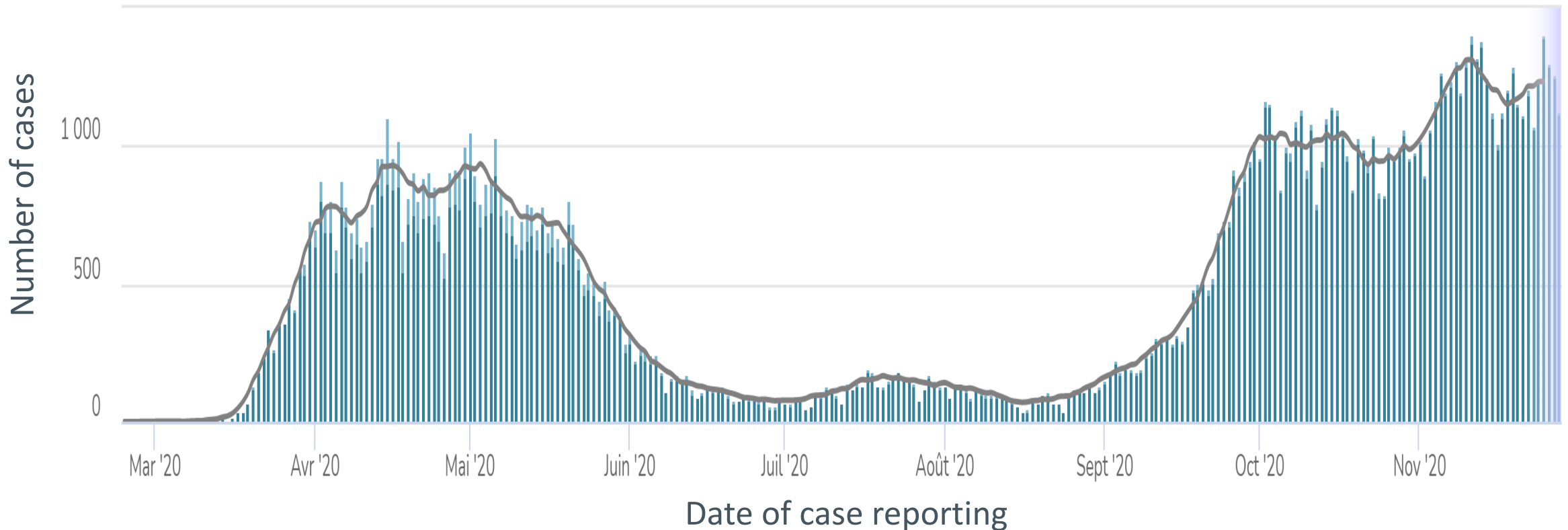


Note: The total number includes publicly reported confirmed and probable cases.

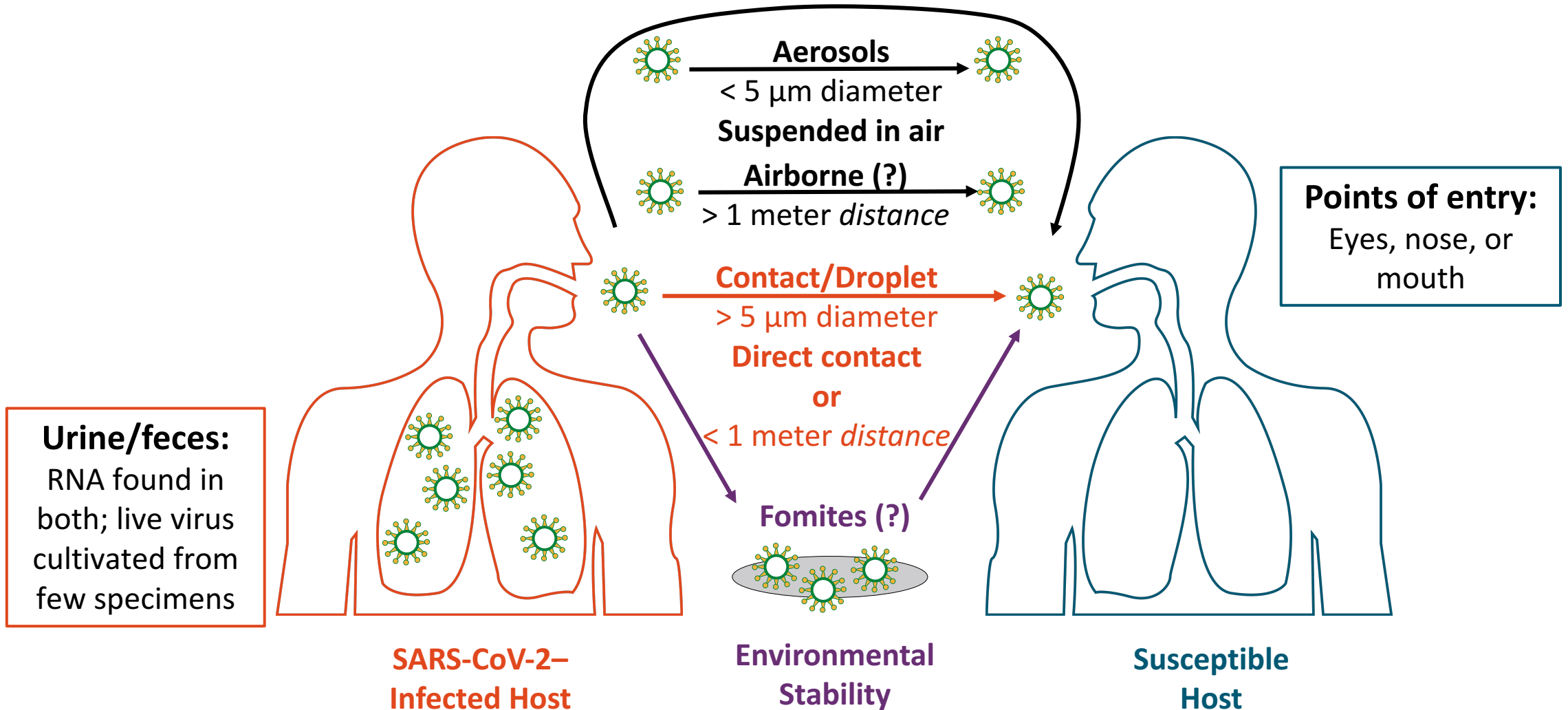
COVID-19 Cases in Quebec March-Nov 2020

Total cases: **134 330**
Montreal cases: **49 029 (36.5%)**

Total deaths: **6 887**
Montreal deaths: **3 596 (52.2%)**

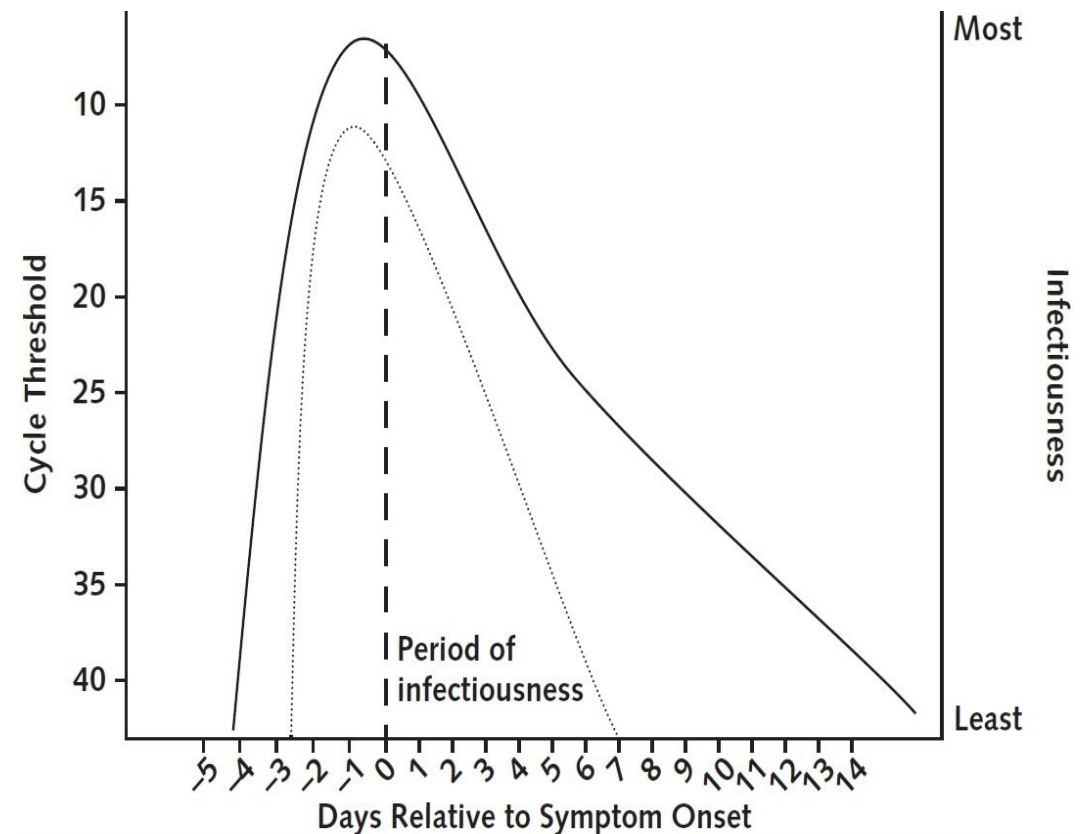


Proposed Routes of SARS-CoV-2 Transmission



COVID-19 Incubation and Infectious Period

- Mean incubation: **5.2 days** (95% CI: 4.1-7.0), up to 14 days
- 97.5% develop symptoms within 11.5 days
- Person-to-person considered predominant mode of transmission, likely via **respiratory droplets** from **coughing, sneezing, or talking**
- Transmission only occurs within the first 6 days of symptoms
- **44%** during pre-symptomatic phase
- Virus **rarely cultured in respiratory samples > 9 days after symptom onset**, especially in patients with mild disease



Risk of Transmission

- Increased with **higher viral load**
- **Indoor >>> Outdoor**; OR=18.7
- Aerosol generating procedures (**singing**) and/or **poor ventilation**
- **Crowding**; Closer proximity <2 meters
- Increases with **longer duration** of contact
- **Super spreader events** account for the majority of transmission
10% of cases account for 80% of secondary cases (China, Israel, Hong Kong)

Transmission Risk in Households and if Asymptomatic

- Household contact attack rate 20%-50%
- Spouse > other household contacts (RR=2.39)
- Household 10X higher than non-household

- 44% of transmissions occur during **pre-symptomatic period**
- In systematic reviews **17% of cases were asymptomatic**
- Risk of transmission is higher if symptomatic vs. asymptomatic (RR=3.23)

Disease Spectrum and Mortality

- **80%** mild-moderate not hospitalized
- **14%** hospitalized
- **5%** critically ill
- Of hospitalized ~15% admitted to the ICU
- Overall case fatality in high income countries: **2.5-3.5%**
- Among cohort China N=44,000, mortality **increased** with **age** and **co-morbidities** (cardiac, diabetes, immunosuppression etc.)

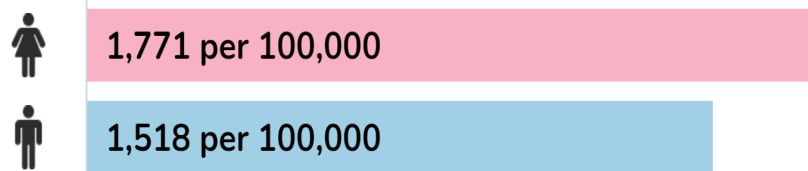
Age Group (yrs)	Mortality %
<40 yrs	0.2
40-49	0.4
50-59	1.3
60-69	3.6
70-79	8.0
>80	14.8

COVID-19 Cases in Quebec: More women, younger age

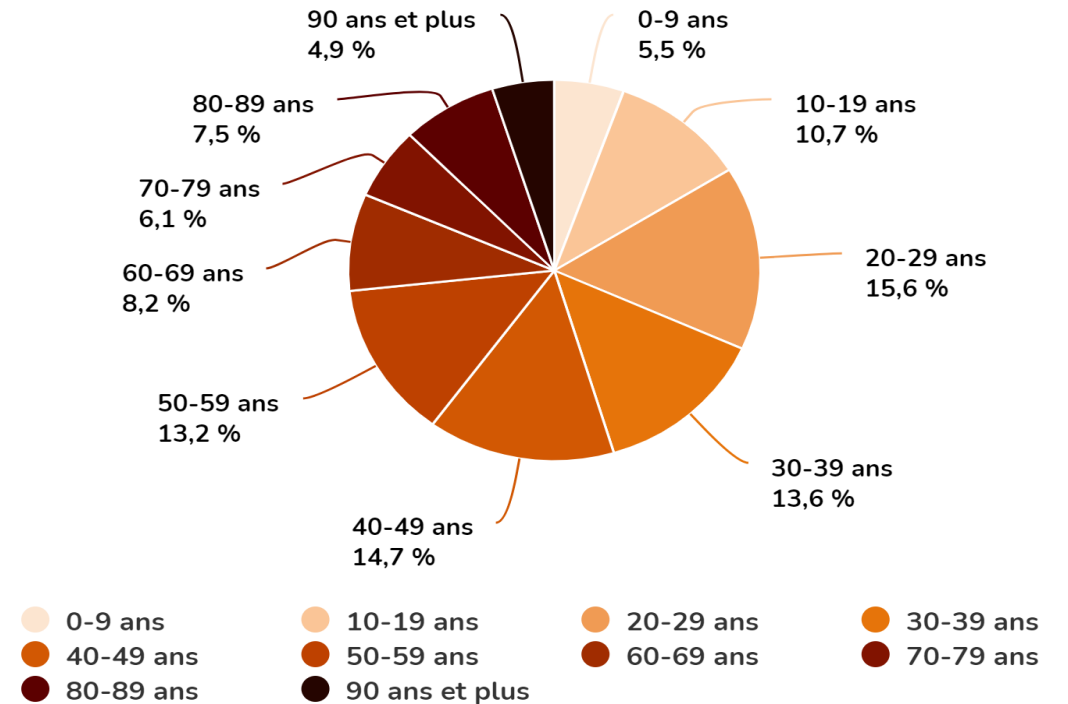
1.1 - Distribution of confirmed cases of COVID-19 in Quebec by sex ■



1.2 - Standardized rates of confirmed cases of COVID-19 in Quebec by sex ■



1.3 - Distribution of confirmed cases of COVID-19 in Quebec by age group ■



COVID-19 Deaths Quebec: Higher males, 73% >80 years

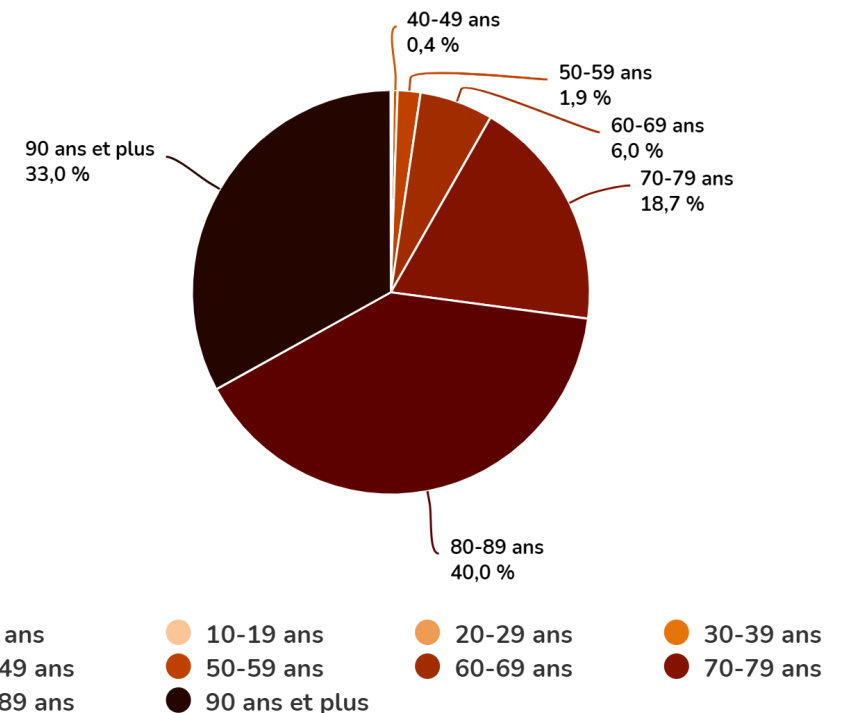
2.1 - Distribution of deaths linked to COVID-19 in Quebec by sex



2.2 - Standardized COVID-19 mortality rates by sex



2.3 - Distribution of deaths linked to COVID-19 in Quebec by age group



COVID-19 Higher Risk in vulnerable populations



Ethnic minorities

- 3x cases
- 2x deaths

Primary Symptoms of COVID-19

17% Asymptomatic

“Symptoms may appear **2-14 days** after exposure to the virus”

Median 5 days
97.5% sx by 11.5 days

Congestion or runny nose,
new loss of taste or smell

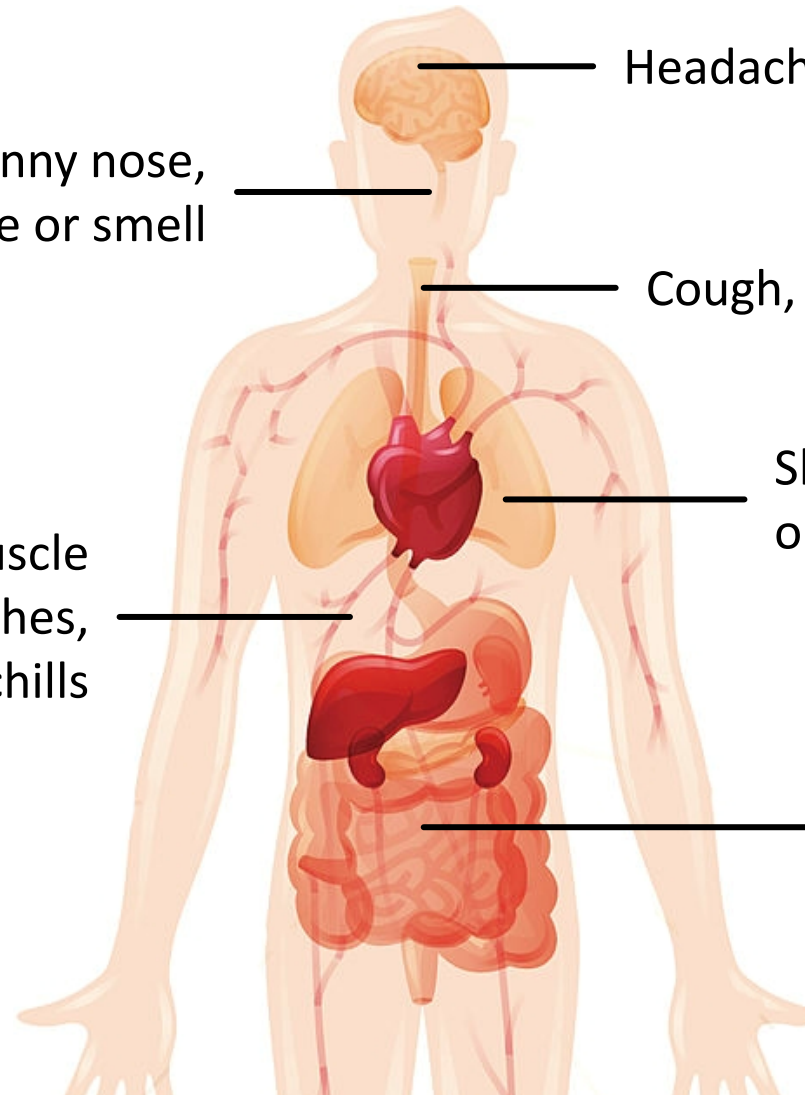
Headache

Cough, sore throat

Shortness of breath
or difficulty breathing

Fatigue, muscle
or body aches,
fever or chills

Nausea or
vomiting, diarrhea



COVID-19 Severity Spectrum

Stage	Characteristics
Asymptomatic or presymptomatic infection	<ul style="list-style-type: none">Positive test for SARS-CoV-2 but no symptoms
Mild illness	<ul style="list-style-type: none">Varied symptoms (eg, fever, cough, sore throat, malaise, headache, muscle pain) but no shortness of breath, dyspnea, abnormal imaging
Moderate illness	<ul style="list-style-type: none">SpO₂ ≥ 94% and lower respiratory disease evidenced by clinical assessment or imaging
Severe illness	<ul style="list-style-type: none">SpO₂ < 94%, PaO₂/FiO₂ < 300, respiratory rate > 30 breaths/min, or lung infiltrates > 50%
Critical illness	<ul style="list-style-type: none">Respiratory failure, septic shock, and/or multiorgan dysfunction

Symptom Spectrum

Mild-Moderate Disease

N=1566, Europe; March 22-April 20,

<10% hospitalized, no- ICU

Mean age: **39 yrs**, **60% female** (31% HCW)

Mean duration Sx: **11.5 days + 5.7 days**

Symptoms	%
Headache	70
Loss of smell (last at least 7 days)	70
Nasal obstruction	68
Fatigue	63
Cough	63
Myalgia	62
Rhinorrhea	60
Loss taste	54
Pharyngitis	53
Fever (> 38°C)	45

Moderate/Severe Hospitalized

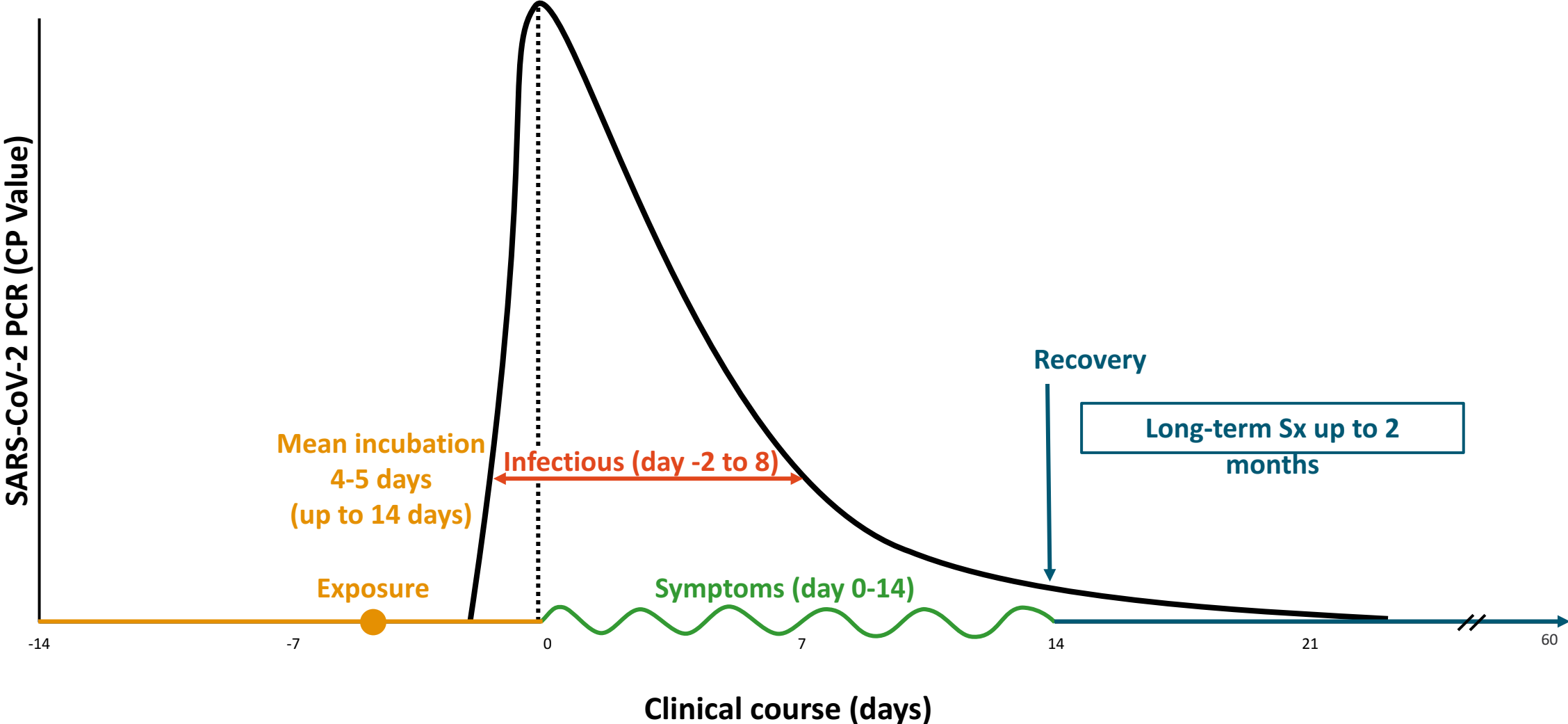
N=20,133 Hosp, UK Feb 6-Apr 19

Median age: **73 yrs** (IQR 58-82), **60% male**

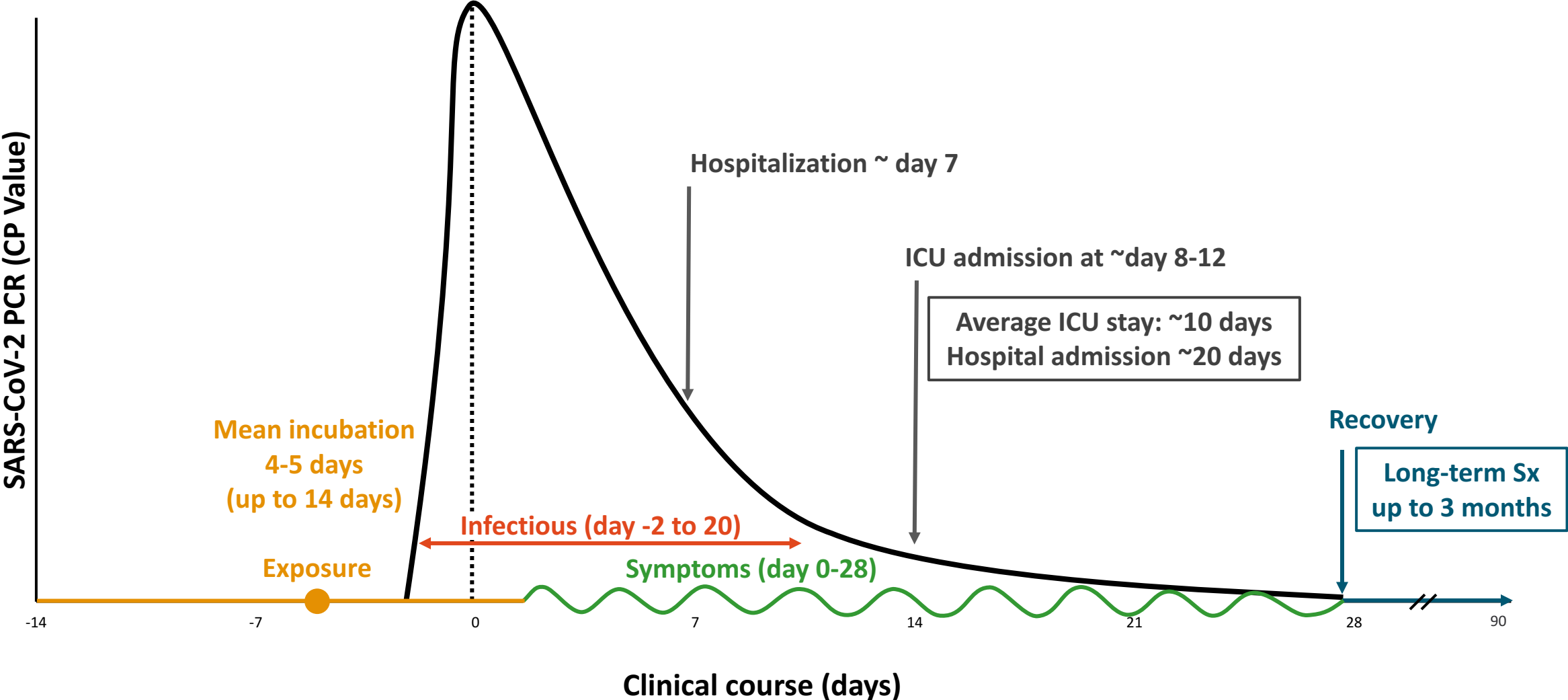
Median duration Sx prior to admission ~7 days

Presenting Symptoms	%
Cough	69
Fever	72
Shortness of breath	71
MSK (myalgia, joint pain, headache, fatigue)	35
Gastrointestinal (abdominal pain, vomiting, diarrhea)	29
Enteric only	4
GI alone more severe and poor disease course (ARDS)	10

Clinical Course Mild COVID-19



Clinical Course Moderate-Severe COVID-19



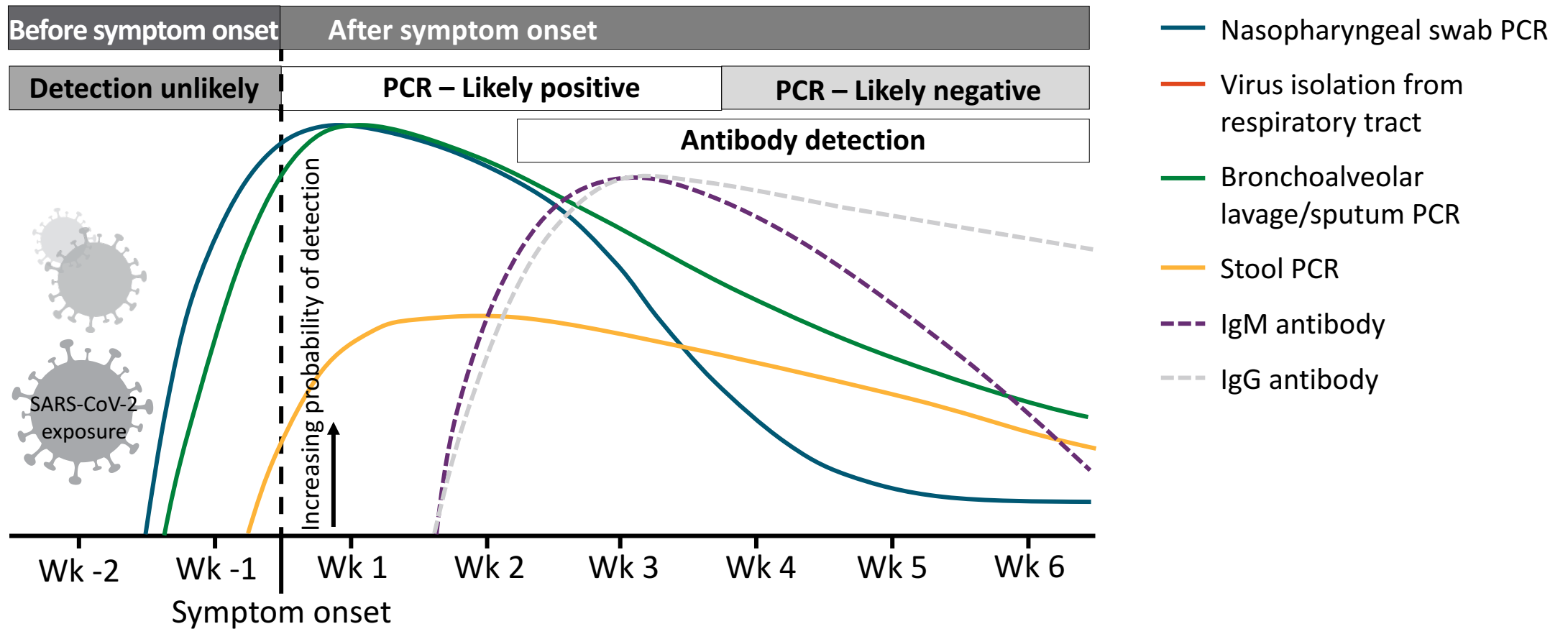
Moderate/Severe COVID-19 Associated Complications/Outcomes

- In hospital complications of heart, brain, lung, kidney and coagulation
 - **Myocarditis, cardiomyopathy, arrhythmias**
 - **Acute cerebrovascular disease** and encephalitis (up to 8%)
 - Venous and arterial and **thromboembolic** events (10%-20%), in the ICU up to 31% to 59%
 - **Hypoxemic resp failure/ARDS** (17%-35%)
 - Acute **kidney injury** (9%), **Liver dysfunction** (19%)
- **17-20%** ICU admission, **~60%** ventilated
- Overall Mortality **21%** (dramatically increases >70 years up to 50%)
- ICU mortality up to 30%

Post-COVID-19 Symptoms (Long Haulers)

- **Common, unclear pathogenesis, unclear management**
- Non-critical COVID-19, N=150, f/u d 7,30 and **60 days**, France
 - Mean age 49 yrs, 54% 1 co-morbidity, 50% HCW
 - **66%** at least one symptom at 2 month (anosmia/ageusia most common)
 - **30%** dyspnea and **40%** fatigue at 2 months
- Hospitalized COVID-19, N= 143, **F/U 60 day**, Italy
 - Mean age 56.5 yrs, 54% O2, 15% non-invasive ventilation, 5% ventilation
 - **83% still had some symptoms** (fatigue and dyspnea), 60 days after symptom onset
 - Most common symptoms fatigue (53%), dyspnea (43%), arthralgias (27%), chest pain (22%)
- Hospitalized COVID-19, N=120, **F/U >3 mo** (mean 111 days), France
 - Mean age 63 yrs, 62% males
 - Most common, Fatigue (55%), dyspnea (41%), memory loss (34%), sleep disorder (31%)

Temporal Considerations for Diagnosis



Sensitivity and Specificity SARS-CoV-2 PCR Based on Clinical Sample Collection

Test, % (95% CI)		Sensitivity	Specificity
Sample location (3 studies)	▪ Upper respiratory tract	76 (51-100)	100 (99-100)
	▪ Lower respiratory tract	89 (84-94)	100 (99-100)
Upper respiratory tract samples (11 studies)*	▪ Oral	56 (35-77)	99 (99-100)
	▪ Nasal	76 (59-94)	100 (99-100)
	▪ Nasopharyngeal	97 (92-100)	100 (99-100)
	▪ Nasal (vs nasopharyngeal)	95 (87-100)	100 (99-100)
	▪ Saliva	85 (69-94)	100 (99-100)
Repeat testing via nasopharyngeal swab (3 studies)	▪ Single test	71 (65-77)	100 (99-100)
	▪ Repeat test	88 (80-96)	100 (99-100)

*Not head-to-head comparisons. Not all specimens were collected from the same patients at the same time point, the time of collection from symptom onset was not provided in all studies, and the studies used various approaches for establishing SARS-CoV-2 positivity to define positive results.

SARS-CoV-2 Diagnostic Testing

- **PCR NPA test of choice for diagnosis**
 - Throat, nose, saliva are less sensitive than NPA
 - Sputum/BAL more sensitive than NPA but reserved if NPA negative
 - PCR on gargle promising- being evaluated
 - Rapid point of care tests not ready for prime time yet
 - Antigen poorly sensitive (~50%)
 - Molecular tests sensitivity range 70-95%, still need NPA, equipment
 - Antibodies not useful in acute diagnosis
 - Positive >1-2 weeks after symptom onset
 - Unclear how well they predict protection
 - Current role is in seroprevalence on population level
-

Key Therapeutic Classes Under Investigation for Treatment of COVID-19

Antivirals

Baloxivir
Convalescent plasma
Favipiravir
(Hydroxy)chloroquine
Interferon
Lopinavir/ritonavir
Nitazoxanide
Oseltamivir
Remdesivir
Ribavirin

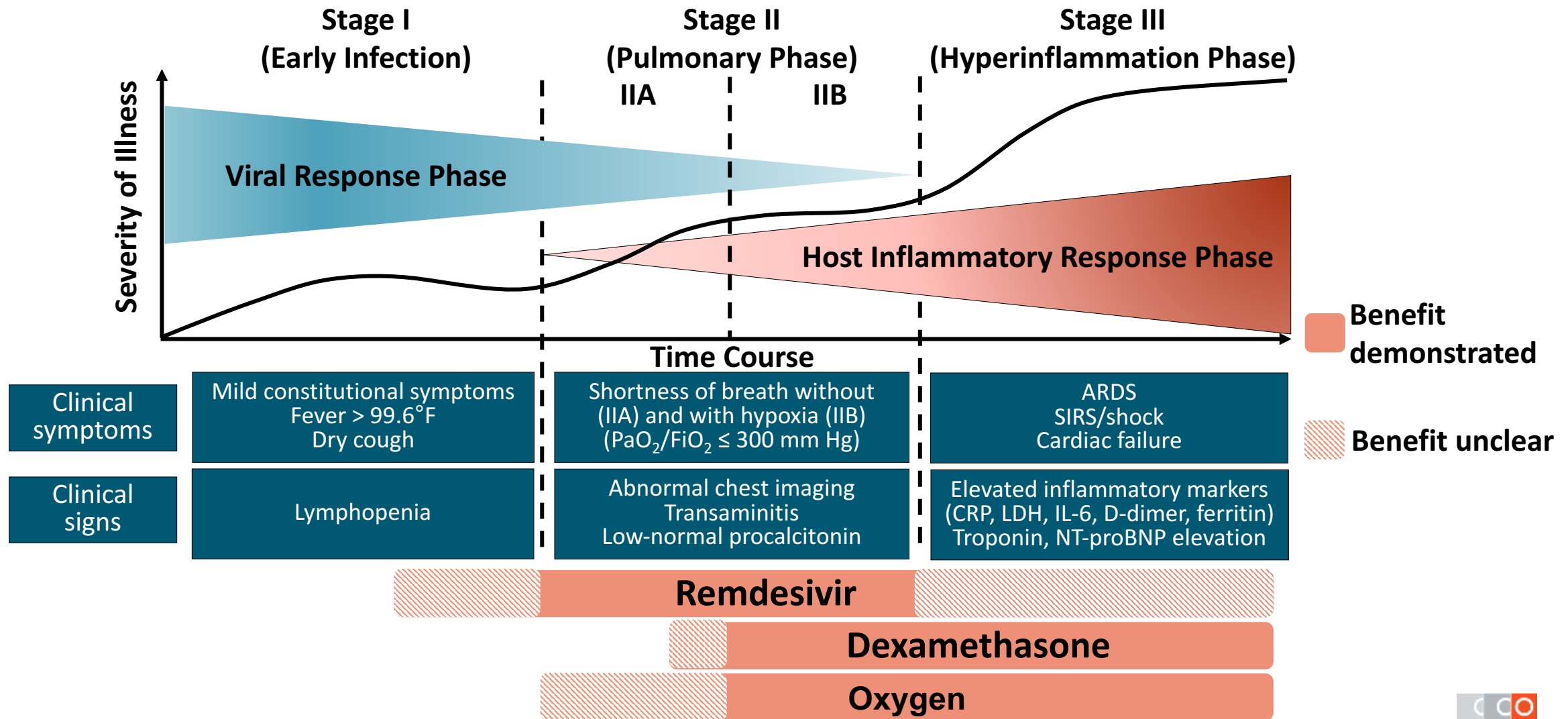
Immunomodulators

Corticosteroids (eg, dexamethasone)
IL-1 inhibitors (eg, anakinra)
IL-6 inhibitors (eg, tocilizumab)
Intravenous immunoglobulin
JAK inhibitors (eg, baricitinib)

Monoclonal antibodies

Bamlanivimab
Casirivimab and Imdevimab

COVID-19 Therapies Predicted to Provide Benefit at Different Stages



COVID-19 Management by Severity of Disease

	Management/Treatment	Infection Control
COVID Contact	<ul style="list-style-type: none"> • Screen for COVID • No post-exposure prophylaxis available 	<ul style="list-style-type: none"> • Isolation x 14 days • Test at 6 days, if positive isolate x 10 days from symptom onset • If negative isolate x 14 days
Mild Disease	<ul style="list-style-type: none"> • Outpatient management • Monitor those with co-morbidities by telemedicine • No antiviral or immunotherapy treatment available 	<ul style="list-style-type: none"> • Home isolation until 10 days after symptom onset and 24 hours fever and improvement in other symptoms • Screen household/close contacts
Moderate disease	<ul style="list-style-type: none"> • No O2 needed, signs/symptoms lower respiratory infection • Consider hospitalization if significant symptoms or risk factors for progression (>70 yrs, comorbidities, immunocompromised) 	<ul style="list-style-type: none"> • If stay at home as mild disease • If hospitalized as severe disease
Severe disease	<ul style="list-style-type: none"> • O2 required, hospitalize • Remdesivir, Dexamethasone 	<ul style="list-style-type: none"> • Isolation until >21 days symptom onset, no acute symptoms 24 hrs, no fever 48 hrs
Critical Disease	<ul style="list-style-type: none"> • ICU admission • ?Remdesivir, Dexamethasone 	<ul style="list-style-type: none"> • Immunosuppressed >28 days or • If >21 and <28 days, two negative COVID tests

COVID-19 VACCINE TRACKER

57
VACCINES

136
TRIALS

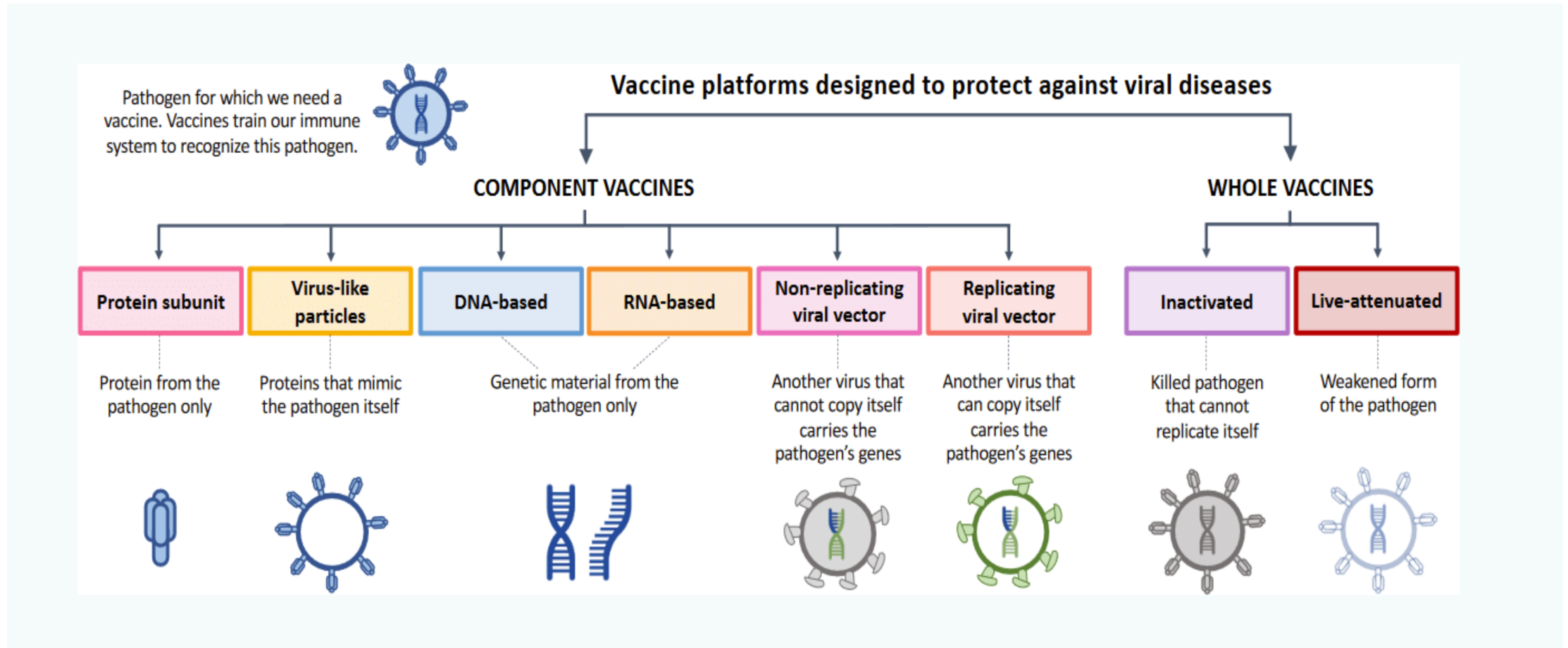
37
COUNTRIES



[About Trial Phases](#) ⓘ

Last Updated 14 November 2020 based on WHO data released 12 November 2020.

Different types of Vaccines



COVID-19 Management Resources

- **IDSA:** <https://www.idsociety.org/covid-19-real-time-learning-network/clinical-guidelines-and-guidance/>
- **NIH:** <https://covid19treatmentguidelines.nih.gov/introduction/>
- **CDC:** <https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html>
- **PHAC:** <https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/clinical-management-covid-19.html#a6>
- **INSPQ:** <https://www.inspq.qc.ca/covid-19>

Questions

