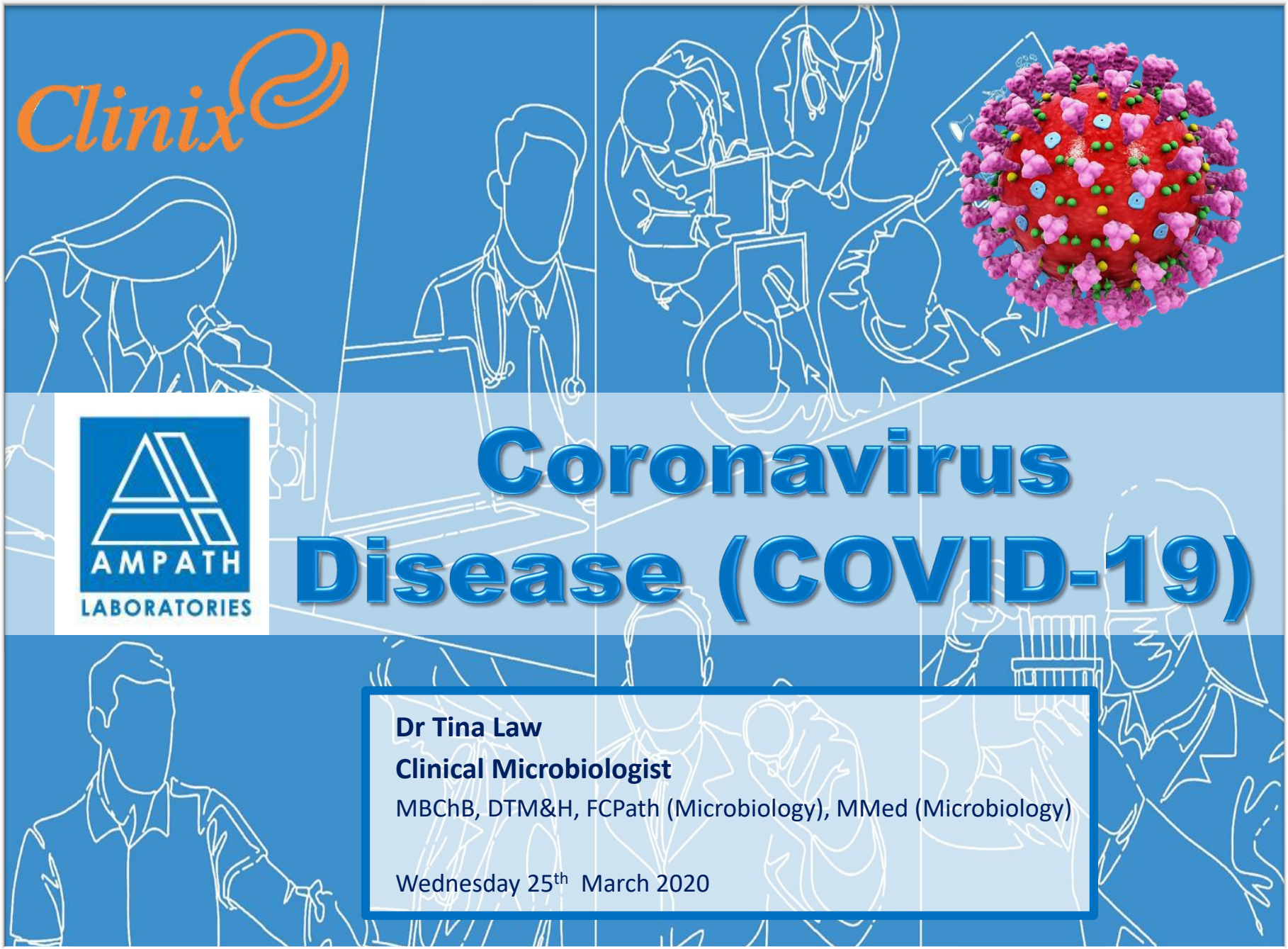
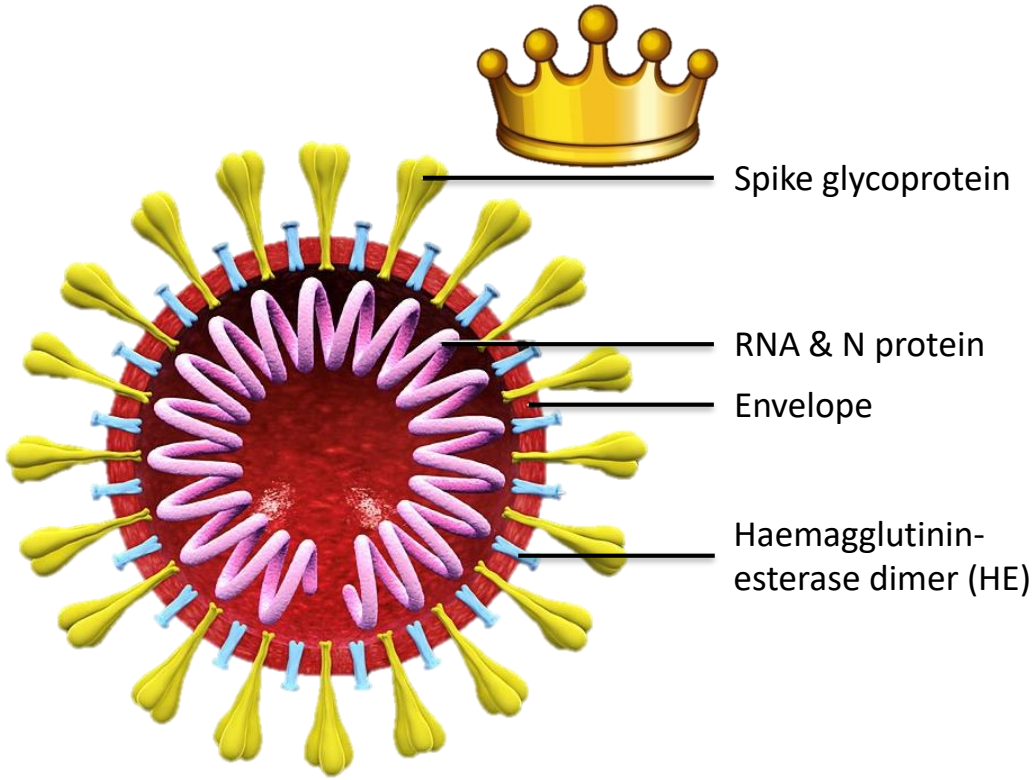
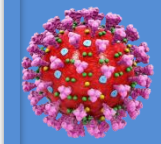

Clinix
AMPATH
LABORATORIES
Coronavirus
Disease (COVID-19)
Dr Tina Law
Clinical Microbiologist
MBChB, DTM&H, FCPath (Microbiology), MMed (Microbiology)
Wednesday 25th March 2020

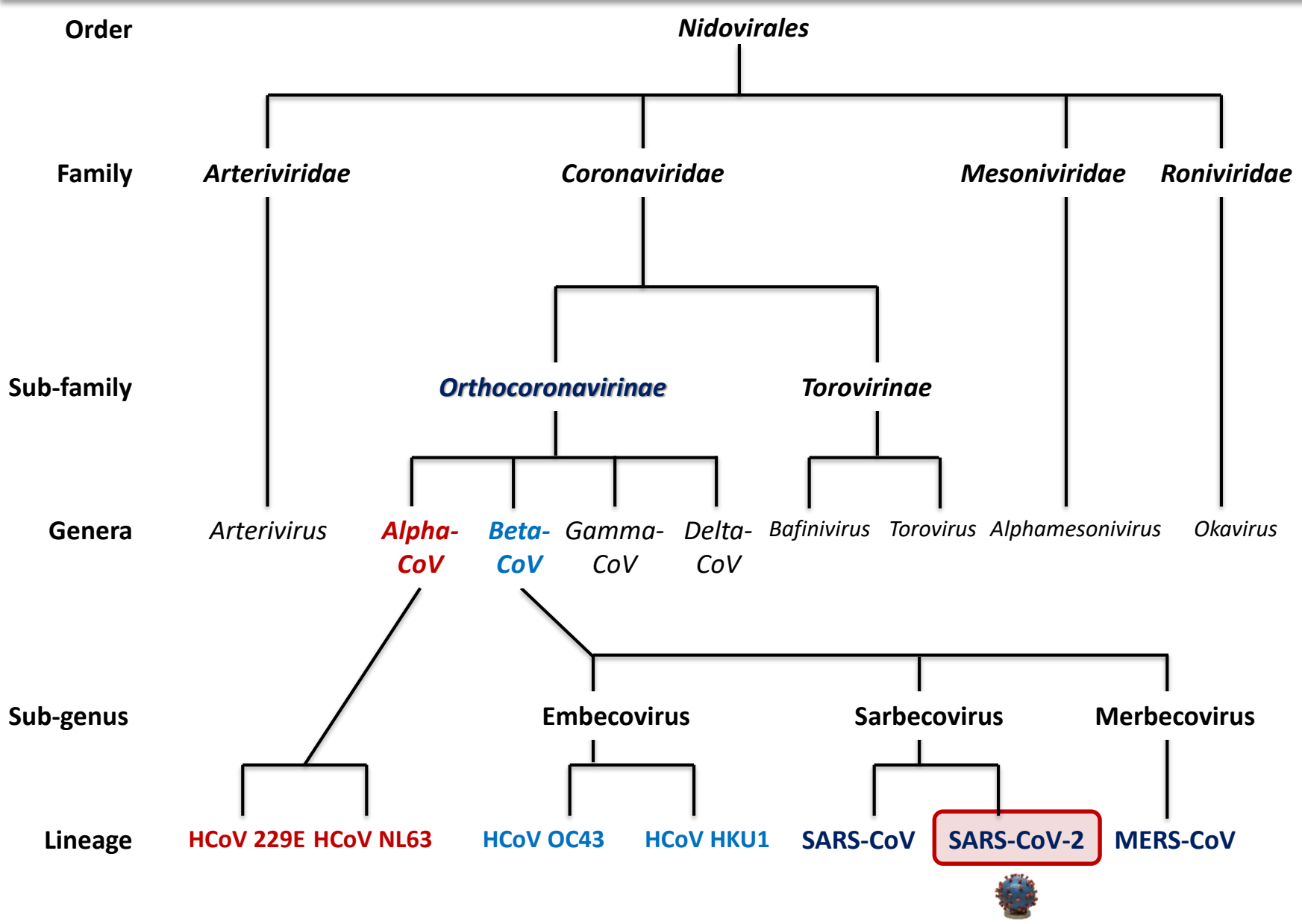
Coronaviruses

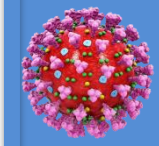
- Coronaviruses are enveloped, single-stranded positive-sense RNA viruses
- Coronavirus envelope is covered with spike glycoproteins which look like 'crowns', on SEM – hence the name 'coronavirus'
- Naturally hosted & evolutionarily shaped by bats
- Group of zoonotic viruses that cause disease in mammals & birds
- In humans, coronaviruses cause self-limited upper respiratory tract infections that are typically mild
- Examples:
  - Coronavirus 229E
  - Coronavirus HKU1
  - Coronavirus OC43
  - Coronavirus NL63
- **3 coronavirus outbreaks:**
  - **SARS-CoV-1**
  - **MERS-CoV**
  - **SARS-CoV-2**





Coronaviruses





Coronavirus Outbreaks

- **2003**: **SARS**

  A new coronavirus emerged in China leading to the SARS (severe acute respiratory syndrome) outbreak
- Vector: Palm civets

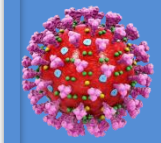
- **2012**: **MERS**

  Another new coronavirus caused Middle East respiratory syndrome (MERS)
- Vector: Dromedary camels

- **2019**, 31 December:

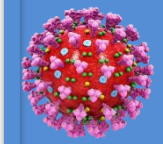
  WHO China office reported a cluster of pneumonia cases in Wuhan, Hubei Province of China
- **2020**, 7 January:

  Causative pathogen was identified as a **novel coronavirus**



Coronavirus Epidemics

	SARS	MERS	COVID-19
Year	2003	2012	2019
Case Fatality Rate	9.6%	34.4%	0.5-4%
Animal reservoir	Bats	Bats	Bats
Animal vector	Palm civets	Camels (Dromedary)	Unknown Possibly pangolin



Coronavirus Outbreaks

- **2020**, 11 February: WHO announced a new name for the disease

According to WHO

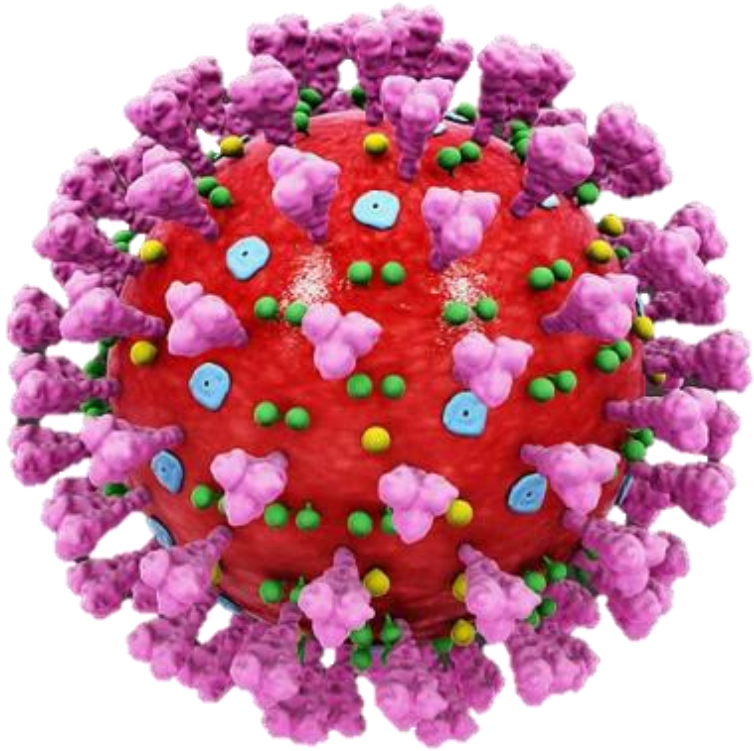
The disease caused by
The Novel Coronavirus

Is officially called

COVID-19

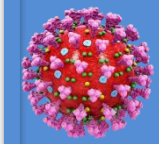
CO – Corona
VI – Virus
D – Disease
19 - 2019

World Health Organization



SARS-CoV-2

- **2020**, 11 March: WHO declared **PANDEMIC**

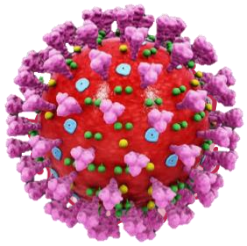


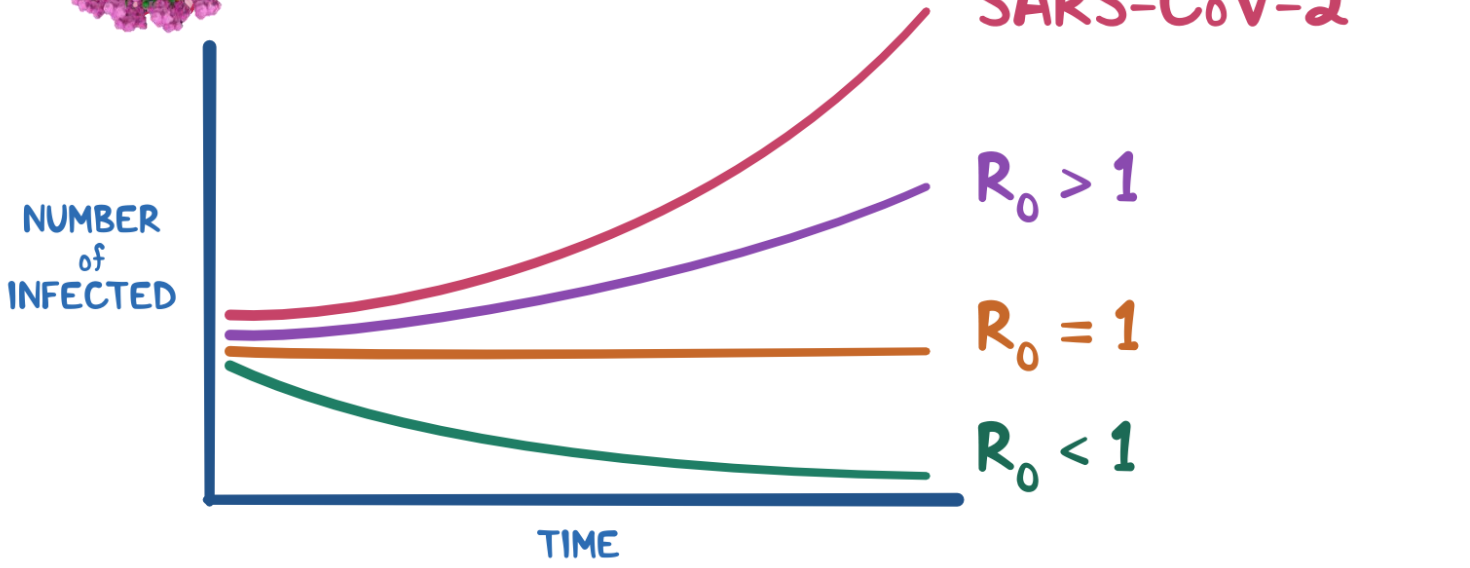


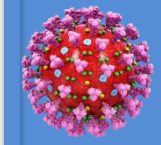
How Infectivity is Measured?

- Scientists use R_0 (reproductive number) to describe the intensity of an infectious disease outbreak
- **Estimated reproductive number for COVID-19 is 2 - 3**

  (on average each infectious case gives rise to 2 to 3 infectious cases)

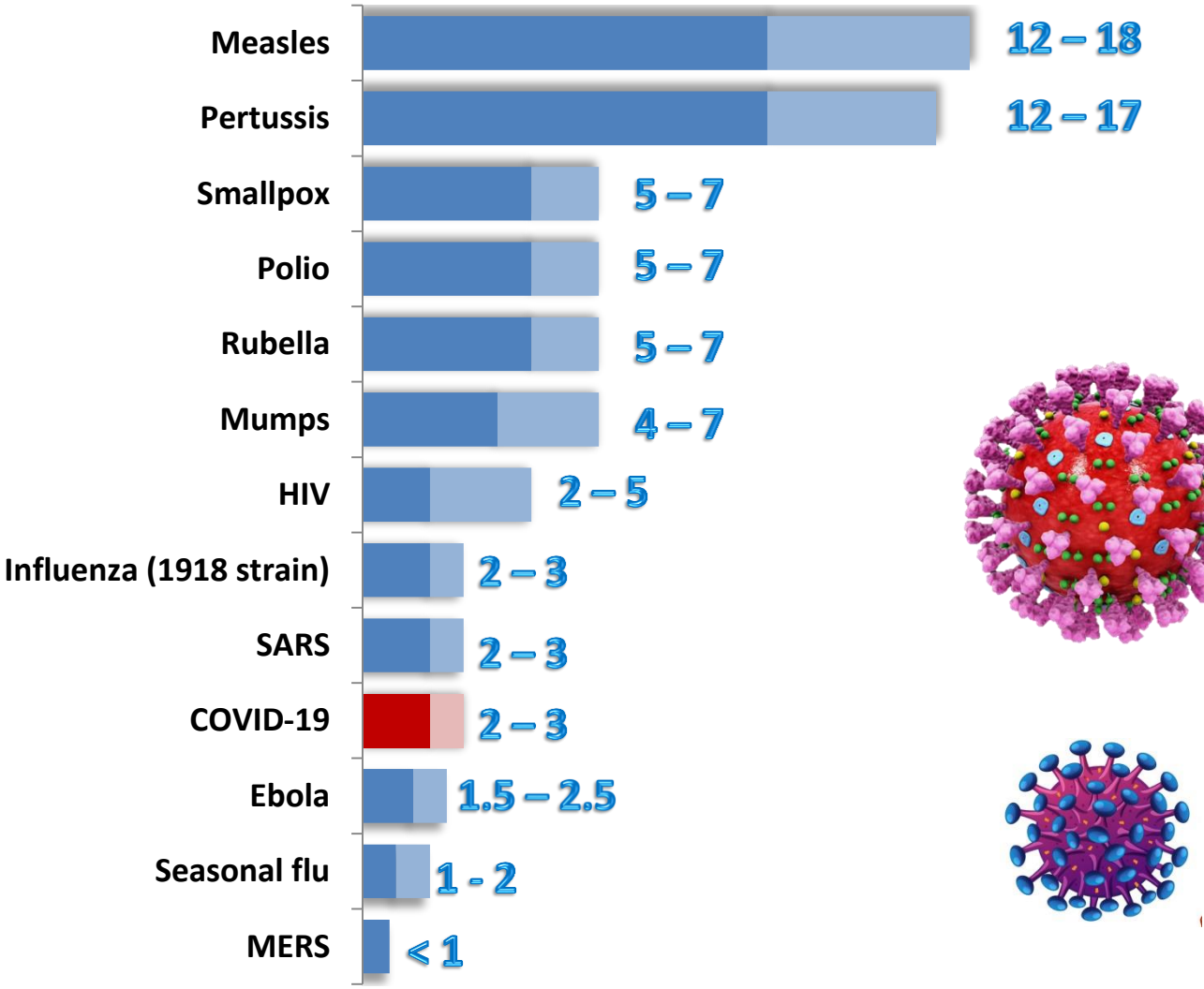


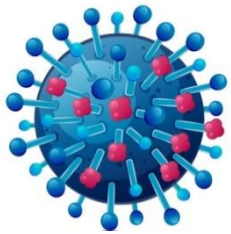


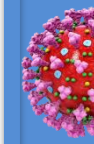


How Contagious is SARS-CoV-2?

Average number of people infected by an individual with the following:

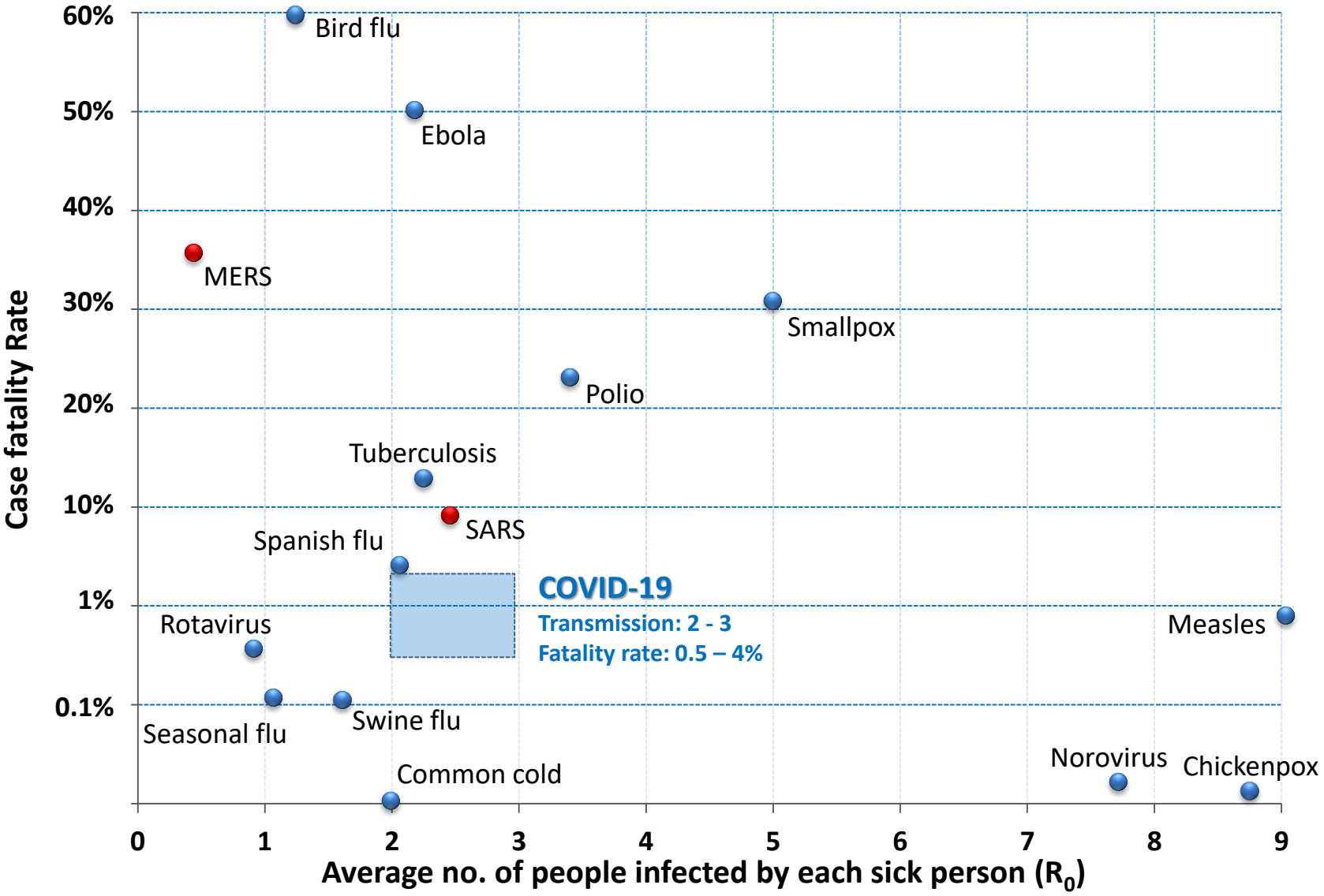


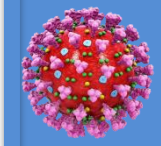




How Contagious & Deadly is it?

- **We don't know exactly, but it's in this range:**

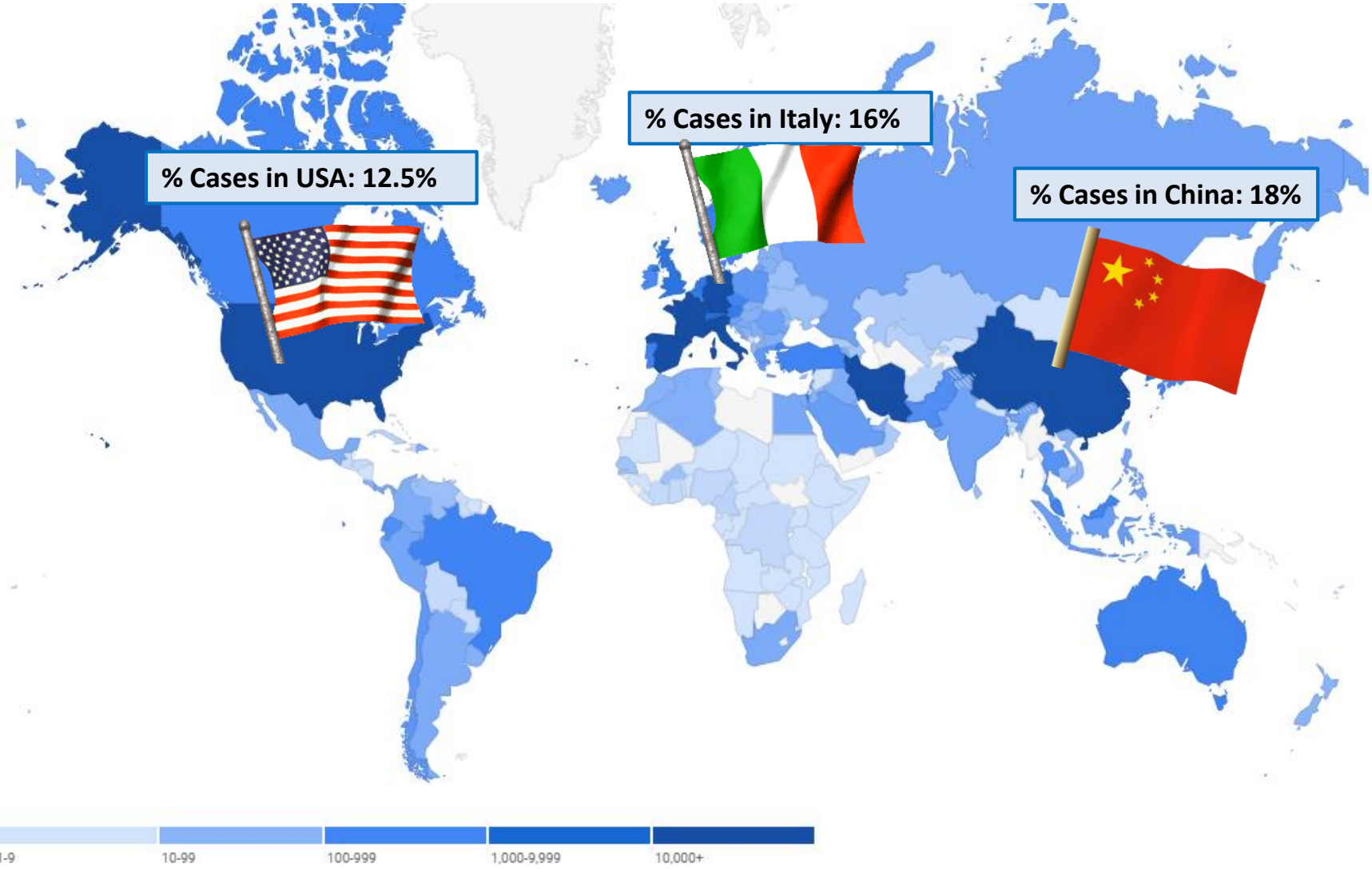




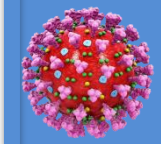
World Coronavirus Dashboard: 25.03.2020

Total Confirmed: 439,940

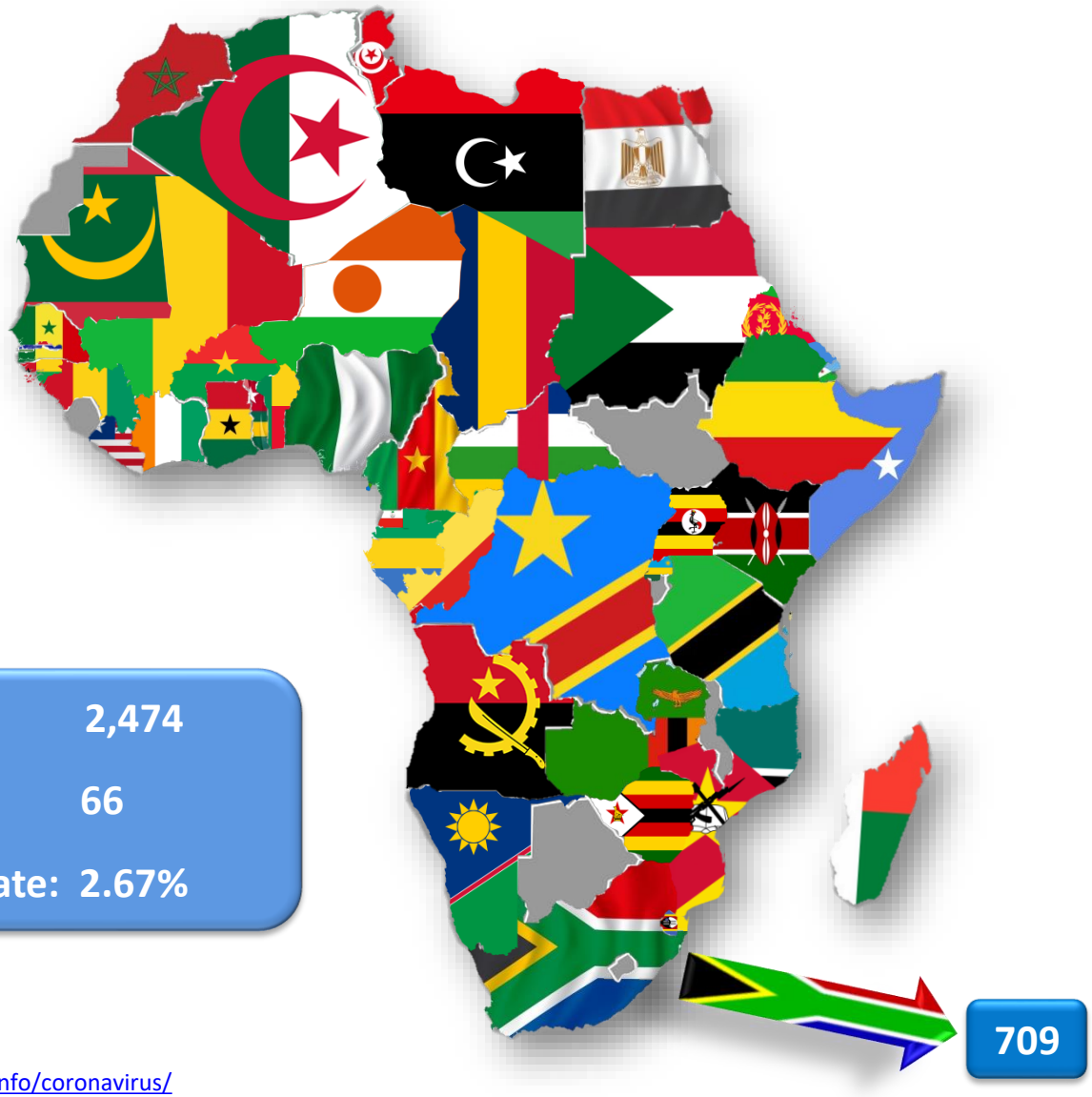
Total Deaths: 19,744



https://www.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6



Africa 25.03.2020: Coronavirus Statistics



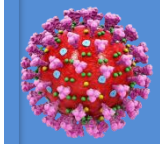
Total Cases:	2,474
Total Deaths:	66
Case fatality rate:	2.67%

https://www.worldometers.info/coronavirus/

South Africa: 25.03.2020

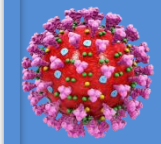
COVID-19 Statistics in South Africa

15529	709	14975	0
COVID-19 Tests Completed	Positive Cases Identified	Negative Cases Identified	Deaths



Transmission

- Main route of transmission is person-to-person spread via **close contact & respiratory droplets** (like the spread of influenza):
  - Coughing
  - Sneezing
- Not airborne transmission
- Viral RNA has been detected: blood, saliva, urine & stool specimens



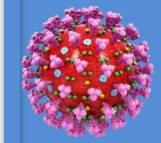
COVID-19 Clinical Features

- Mean incubation period 4 - 5 days (Range: 2 - 14 days)

Typical Symptoms

- 80% of symptomatic cases are mild
- Initially flu-like symptoms - fever, followed by a dry cough
- After 1 week, can lead to shortness of breath, with about 20% of patients requiring hospital treatment
- Rarely seems to cause a runny nose
- Pneumonia is the most frequent manifestation of infection
  - Characterised by fever, cough, & dyspnoea
  - Abnormalities on imaging:
    - CXR : 60-77%
    - Chest CT : 85-95%

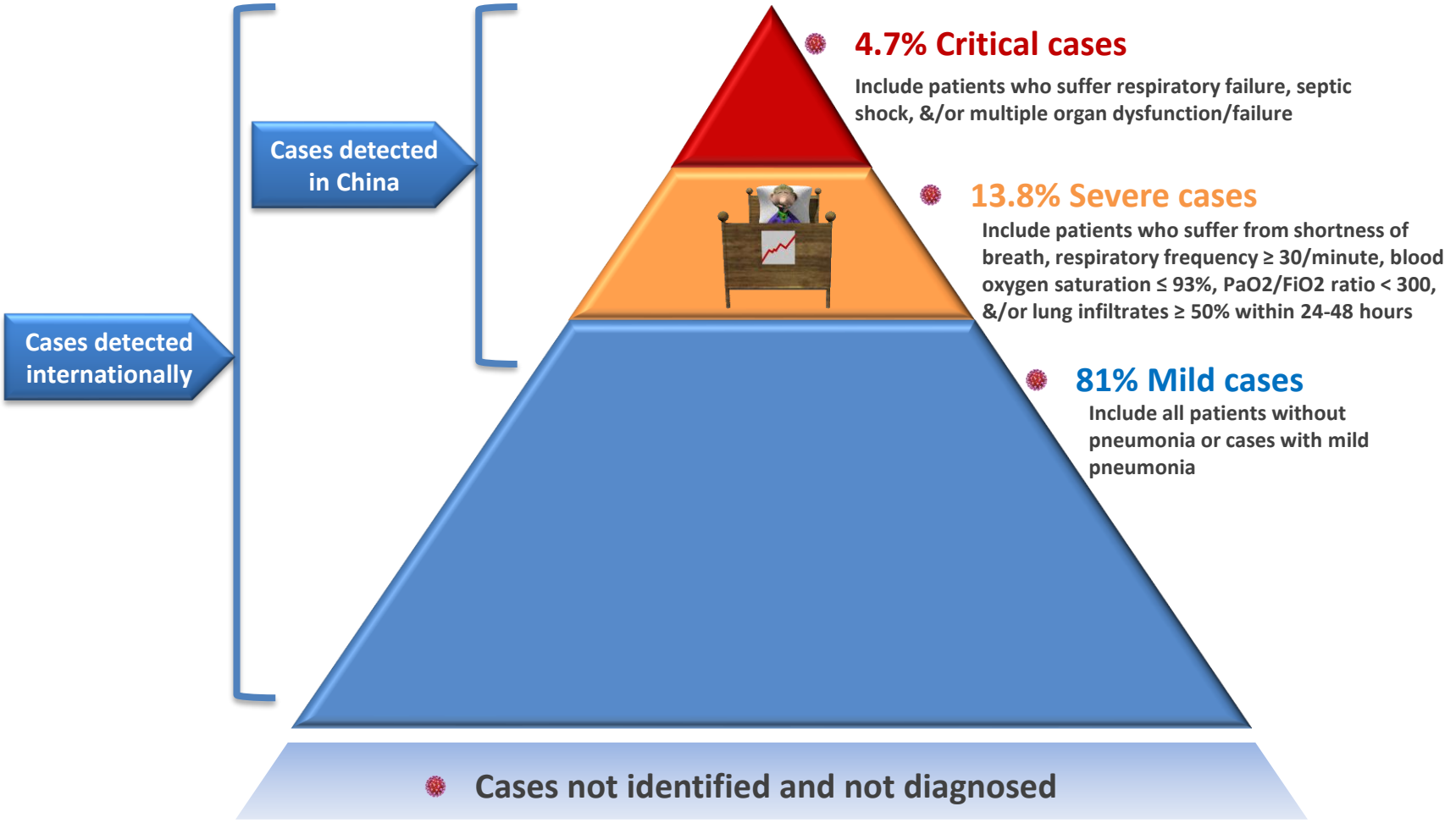
Symptoms[1]	
Cough	68%
Fever (on admission)	44%
Fatigue	38%
Sputum production	34%
Dyspnoea	19%
Myalgia or arthralgia	15%
Sore throat	14%
Headache	14%
Chills	11.5%
Nausea or vomiting	5%
Diarrhoea	4%



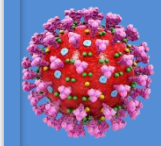
1. Guan W, et al. Clinical characteristics of coronavirus disease 2019 in China. NEJM 2020. DOI: 10.1056/NEJMoa2002032

COVID-19 Severity of Cases

- **Case fatality ratio: 0.5% – 4%**



Data source: China CDC



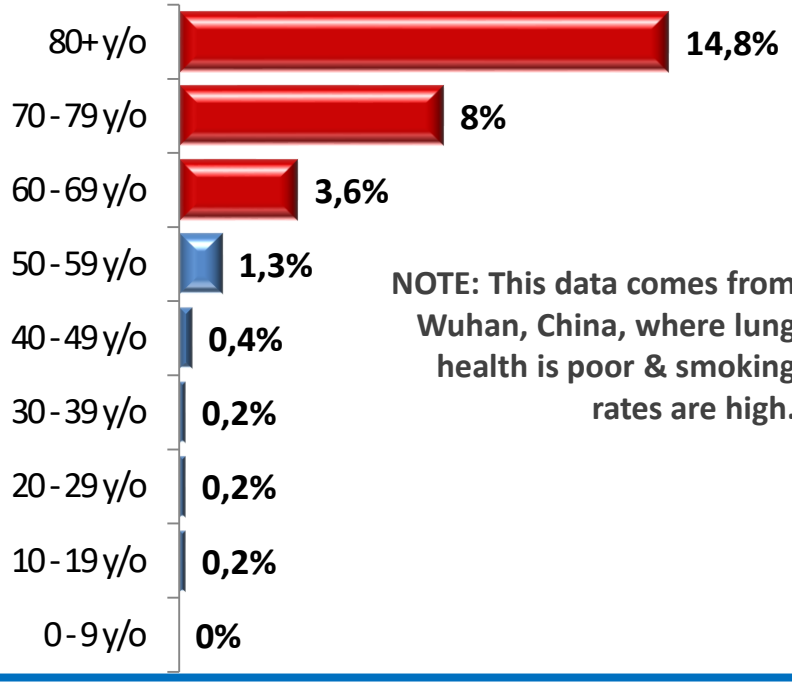


COVID-19 Mortality Rate

- Case fatality ratio currently unknown, but estimated to be **0.5 – 4%**
- In emerging viral infection outbreaks the case-fatality ratio is **often overestimated in the early stages because case detection is highly biased towards the more severe cases**

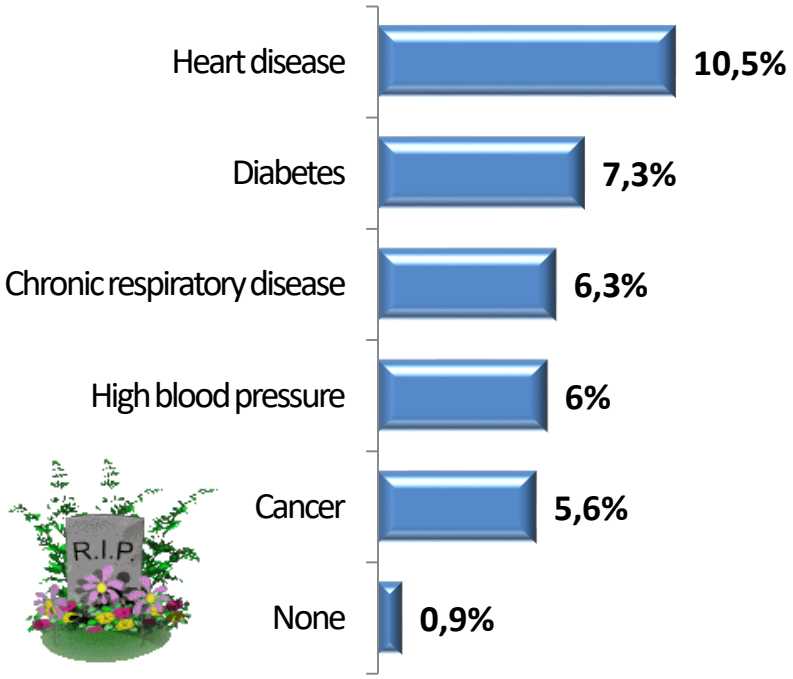
Study: COVID-19 Fatality Rate by Age

Mortality Risk Highest In The Elderly

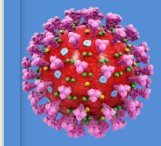


NOTE: This data comes from Wuhan, China, where lung health is poor & smoking rates are high.

Study: COVID-19 Fatality Rate by Pre-existing Conditions

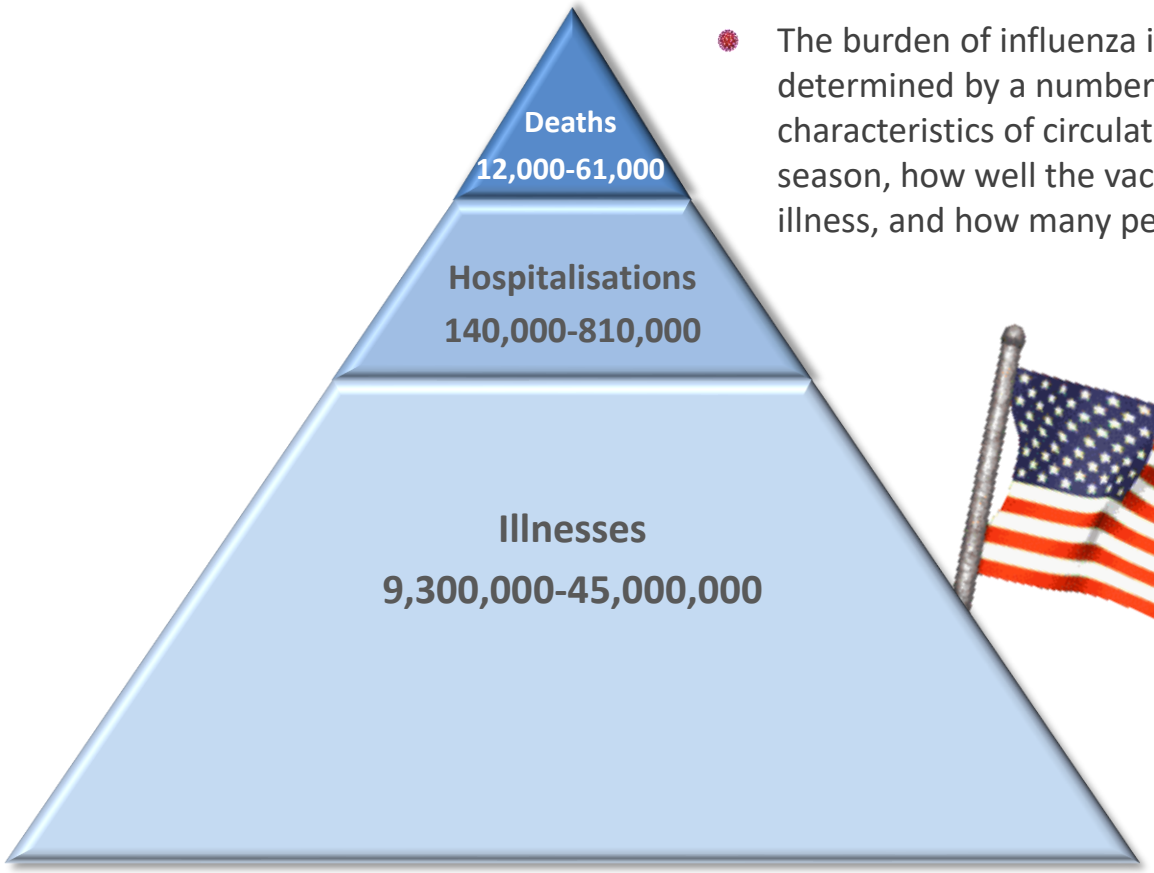


A paper by the Chinese CCDC released on Feb. 17, which is based on **72,314 confirmed, suspected, and asymptomatic cases** of COVID-19 in China as of Feb. 11, and was published in the Chinese Journal of Epidemiology.



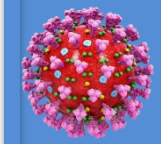
Mortality Rate – In Perspective

- **Estimated Range of Annual Burden of Influenza in the U.S.**

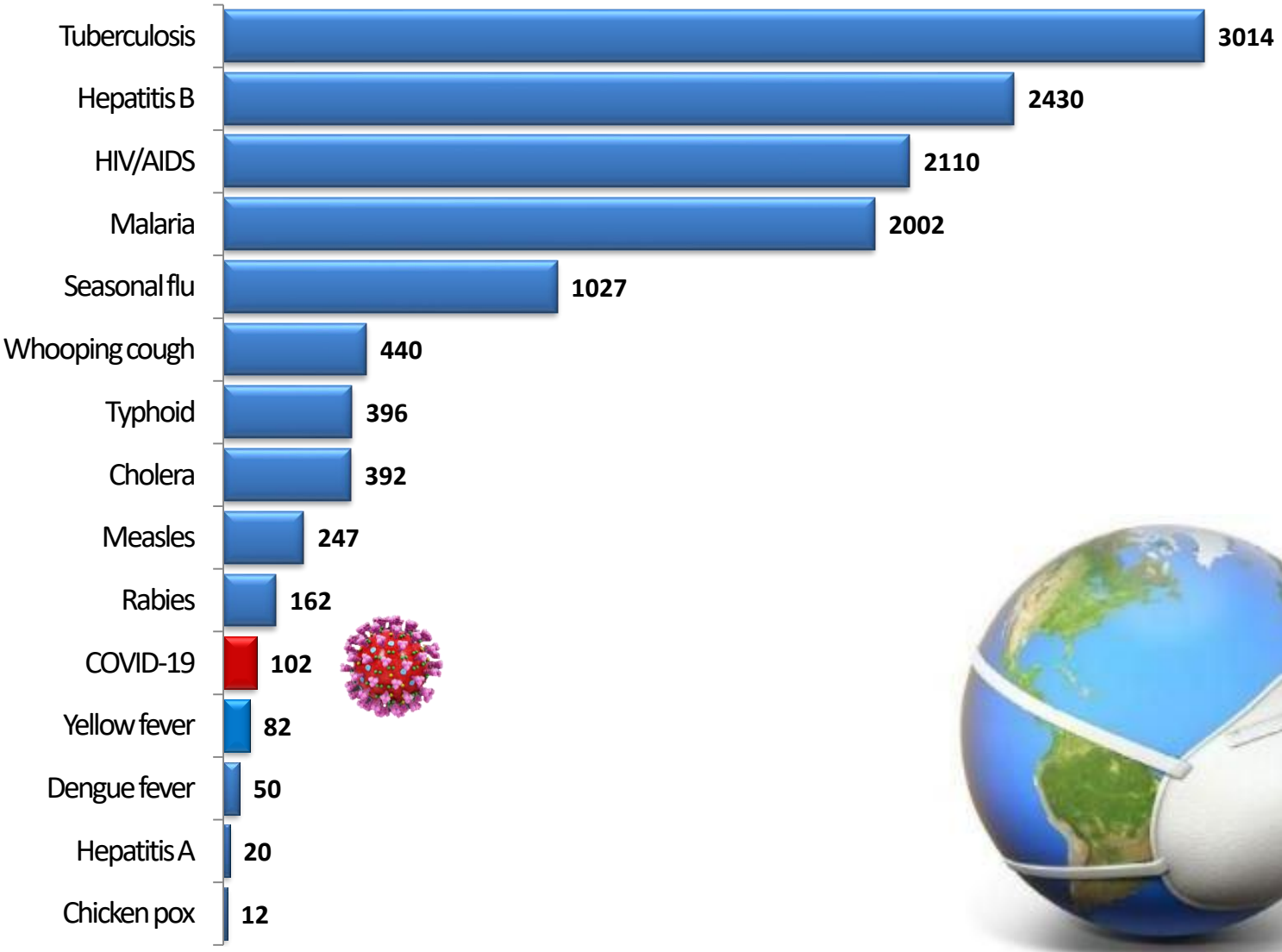


- The burden of influenza in the US can vary widely & is determined by a number of factors including the characteristics of circulating viruses, the timing of the season, how well the vaccine is working to protect against illness, and how many people got vaccinated

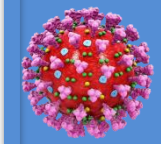
Data source: U.S. CDC



Disease Deaths per Day Worldwide

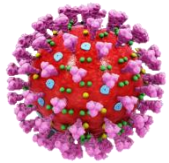


Data source: U.S. CDC, WHO, The Lancet



Who Qualifies for Testing for COVID-19?

Persons with acute respiratory illness, with sudden onset of at least one of the following: cough, sore throat, shortness of breath or fever [≥ 38°C (measured) or history of fever (subjective)] irrespective of admission status



AND

In the 14 days prior to onset of symptoms, met at least one of the following epidemiological criteria:

- Were in close contact[1] with a confirmed[2] or probable[3] case of SARS-CoV-2 infection

OR

- Had a history of international travel

OR

- Worked in, or attended a health care facility where patients with SARS-CoV-2 infections were being treated

OR

- Admitted with severe pneumonia of unknown aetiology

[1] **Close contact:**

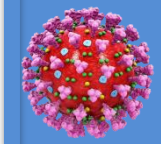
- A person having had face-to-face contact or was in a closed environment with a COVID-19 case; this includes, amongst others, all persons living in the same household as a COVID-19 case and, people working closely in the same environment as a case. A healthcare worker or other person providing direct care for a COVID-19 case, while not wearing recommended PPE (e.g., gowns, gloves, NIOSH-certified disposable N95 respirator, eye protection). A contact in an aircraft sitting within 2 seats (in any direction) of the COVID-19 case, travel companions or persons providing care, & crew members serving in the section of the aircraft where the index case was seated.

[2] **Confirmed case:**

- A person with laboratory confirmation of SARS-CoV-2 infection, irrespective of clinical signs and symptoms

[3] **Probable case:**

- A PUI for whom testing for SARS-CoV-2 is inconclusive (the result of the test reported by the laboratory) or for whom testing was positive on a pan-coronavirus assay



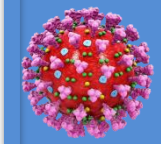
Who Should be Tested?

- The only persons who should get testing for COVID-19 are those described in the previous slide under '*Person Under Investigation (PUI)*'

- **If you are unsure whether you qualify for testing, call:**

Public Hotline:
0800 029 999
0800 111 132
Public WhatsApp:
0600 123 456

Clinicians Hotline:
0800 111 131





Testing for COVID-19

- All persons under investigation require testing for SARS-CoV-2 by means of reverse transcriptase PCR (RT-PCR)

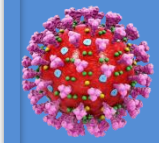
NEW!

- Samples to be sent are:
  1. *Upper respiratory tract samples* – nasophargyngeal & oropharyngeal swabs in all patients

Turn Around Time: 24 hours

AMPATH

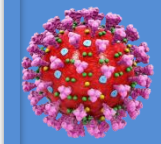
  2. *Lower respiratory tract samples* – may not be possible depending on the patient's symptoms. Where available, send sputum, tracheal aspirates, or bronchoalveolar lavage fluid. Sputum induction should not be performed.



Suspected COVID-19 Cases

- **Any patient who fulfils criteria for a suspected COVID-19 case should immediately have the following measures taken:**

  - Give the patient a surgical mask
  - Direct the patient to a separate area, preferably an isolation room if available. Where an individual isolation room is not available, a 1-2m distance should be kept between suspected COVID-19 cases & other patients
  - Instruct the patient to cover their nose & mouth during coughing/sneezing with a tissue or flexed elbow. Patient should perform hand hygiene after contact with respiratory secretions (wash hands or use alcohol-based hand rub, which should be readily available at the point of triage)
  - Limit the movement of the patient (e.g. use portable CXR rather than sending patient to X-ray department). If patient has to be moved, ensure they wear a mask
  - The patient should have a dedicated bathroom (where this is possible)
- **Patients should be quickly triaged in terms of clinical severity**
  - It allows for rapid initiation of supportive therapy (e.g. O_2 supplementation)
  - Patient's with mild symptoms can be allowed home to await results of testing
  - It protects both patients and staff



COVID-19: IPC Strategies for HCWs

- Overuse of PPE will have a further impact on supply shortages
- The following recommendations ensure that PPE is used rationally:
  - Type of PPE used when caring for COVID-19 patients will vary according to the setting & type of personnel & activity
  - HCWs involved in direct care of patients should use the following PPE:

    ➔ Contact: gowns/apron, gloves,
    ➔ Droplet: medical mask, eye protection

  - HCWs involved in aerosol-generating procedures (e.g., tracheal intubation, non-invasive ventilation, tracheostomy, CPR, manual ventilation before intubation, bronchoscopy[1]):

    ➔ N95 respirators, eye protection, gloves & gowns; aprons should also be used if gowns are not fluid resistant

  - N95 respirators can be used for an extended time as PPE is in short supply (8 hours) - wear the same respirator when caring for multiple patients who have the same diagnosis without removing it

1. Tran K, et al. Aerosol-generating procedures and risk of transmission of acute respiratory diseases: a systematic review. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2011.

Management of Confirmed Cases

- **Rapid triage of cases** – in order that appropriate IPC measures & appropriate level of supportive care can be commenced
  - Cases triaged as having moderate or severe disease will require admission for medical reasons
  - Patients with mild disease should be managed at home, provided they are able to safely self-isolate & are not at risk of developing severe disease

- **Criteria for management at home (for age > 12 years)**

Mild disease

- SpO2 ≥ 95%
- Respiratory rate < 25
- HR < 120
- Temperature 36-39°C
- Mental status normal

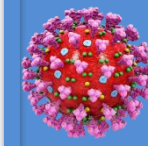
For age 5-12, use respiratory rate < 30, & HR < 130. For younger ages, use age-appropriate normal values

Able to safely self-isolate

- Separate bedroom available for patient to self-isolate in
- Patient able to contact, and return to, healthcare facility in case of deterioration

Not at high risk of deterioration

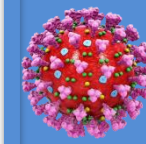
- Age < 65 years
- No cardiac or pulmonary comorbidities
- No other debilitating comorbities (e.g. cancer)





Management of Hospitalised Cases

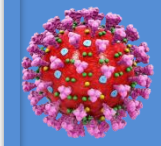
- **Early supportive therapy in hospitalised COVID-19 patients**
- **Give supplemental oxygen therapy immediately to patients with low oxygen saturation**
  - Oxygen therapy is likely to be the single most effective supportive measure in in COVID-19 patients overall
  - Target SpO_2 ≥90% in non-pregnant adults & SpO_2 ≥92-95 % in pregnant patients
  - Children with emergency signs should receive oxygen therapy during resuscitation to target SpO_2 ≥94%; otherwise, the target SpO_2 is ≥90%
- **Use conservative fluid management in patients with severe acute respiratory infections when there is no evidence of shock**
- **If a clinical suspicion for co-infection exists, consider empiric antimicrobials to treat potential co-pathogens, particularly in severe cases**
- **Closely monitor patients with for signs of clinical deterioration, such as rapidly progressive respiratory failure & sepsis, & apply supportive care interventions immediately**



Specific Therapies

- **Do not routinely give systemic corticosteroids for treatment of COVID-19 unless they are indicated for another reason**
- **There is no current evidence from RCTs to recommend any specific treatment for patients with suspected or confirmed COVID-19 infection**
  - This is however, an area of active study
- Candidate drugs undergoing investigation include:
  - Remdesivir
  - Lopinavir/ritonavir (Kaletra©/Aluvia©)
  - Chloroquine
  - Interferon
  - Toculizumab

- To date, published clinical data on most of these agents consists largely of in vitro studies, with little or no human data





Specific Therapies

- Given the state of evidence, the difficulties in procuring many of these agents in South Africa, & drug-drug interactions between chloroquine & lopinavir/ritonavir, we suggest consideration of the following:

Severe disease

- Consider treatment with chloroquine

Mild disease with risk factors for severe disease*

- Consider treatment with chloroquine

Mild disease without risk factors for severe disease

- No treatment recommended

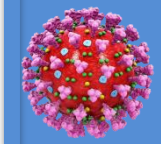
*Risk factors for severe disease are age >65 years, or underlying cardiac or pulmonary disease

Drug	Suggested dosing regimen	Comment
Chloroquine	10 mg/kg base daily for 2 days, then 5 mg/kg base daily for 1 day	Watch QTc, check for drug-drug interactions

- **There is no evidence for the use of any drug or vaccine to prevent COVID-19 infection.** Prevention consists of non-pharmaceutical interventions, such as good hand hygiene and social distancing.

Chloroquine

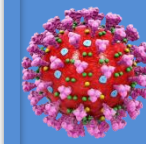
- Mechanism: Immune suppression
- Reduces autophagy, interferes with TLR signaling & decreases cytokine production
- May also interfere with glycosylation of SARS-CoV-2 cellular receptors & prevent virus/cell fusion by increasing endosomal pH



De-isolation Criteria

Asymptomatic patient	De-isolate 14 days after initial positive test
Mild disease	De-isolate 14 days after symptom onset
Severe disease	De-isolate 14 days after clinical stability achieved

- Patients admitted to hospital can continue their isolation period at home once clinical stability has been achieved



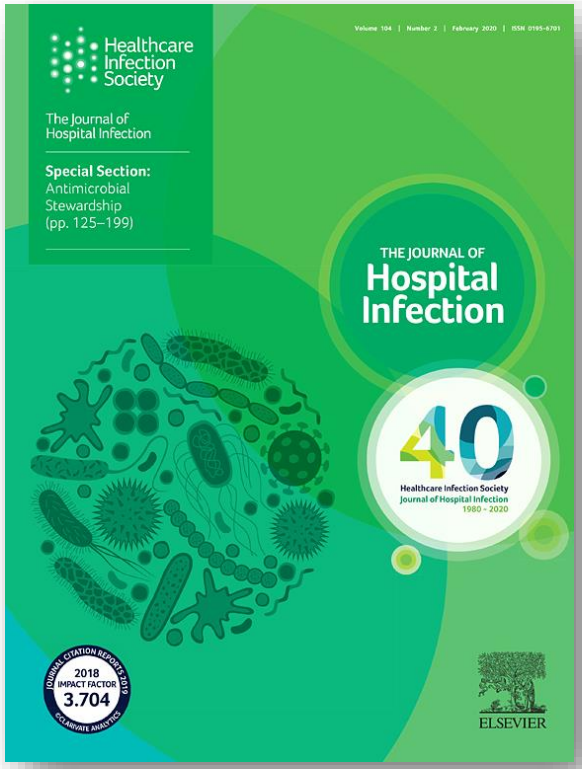

Persistence of Coronaviruses on Surfaces

J Hosp Infect. DOI: https://doi.org/10.1016/j.jhin.2020.01.022

Note: Coronavirus activity may be impacted by temperatures higher than 30°C. SARS-CoV-2 was NOT included in this study.

Persistence of Coronaviruses on Surfaces

- Analysis of 22 studies reveals that human coronaviruses such as SARS-CoV-1, MERS-CoV & endemic human coronaviruses (HCoV) can be efficiently inactivated by surface disinfection procedures within 1 minute when using:
  - **62–71% ethanol**
  - **0.5% hydrogen peroxide**
  - **0.1% sodium hypochlorite**



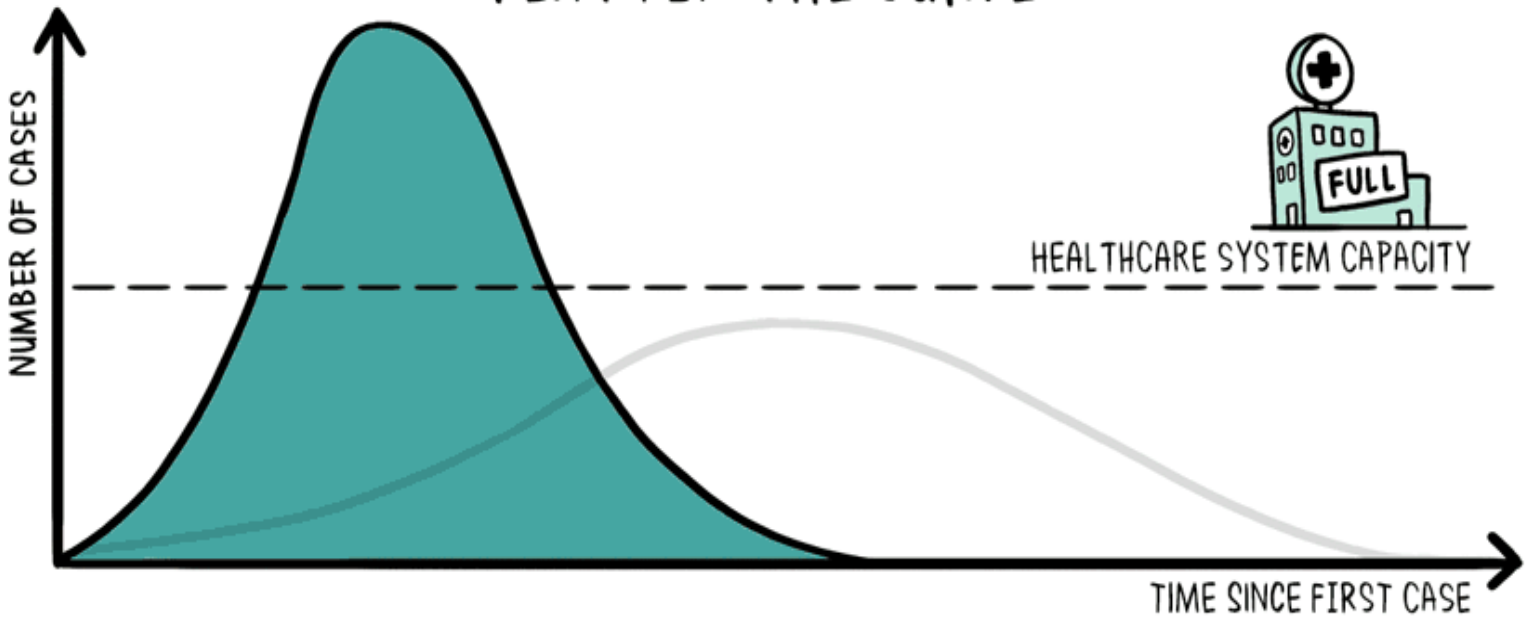
- Other biocidal agents such as 0.05–0.2% benzalkonium chloride or 0.02% chlorhexidine digluconate are less effective

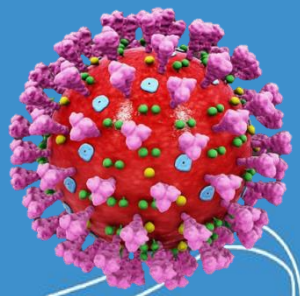
J Hosp Infect. DOI: https://doi.org/10.1016/j.jhin.2020.01.022
Note: Coronavirus activity may be impacted by temperatures higher than 30°C. SARS-CoV-2 was NOT included in this study.

Useful Links

- Coronavirus COVID-19 Global Cases by Johns Hopkins CSSE
  https://www.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6
- WHO Dashboard
  https://experience.arcgis.com/experience/685d0ace521648f8a5beeeee1b9125cd
- NICD website
  http://www.nicd.ac.za/diseases-a-z-index/novelcoronavirus-infection/
- DoH website
  https://www.sacoronavirus.co.za
- www.ampath.co.za

FLATTEN THE CURVE





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ANY QUESTIONS