Protecting the value of access to care during and after the COVID-19 pandemic across Europe: focus on antivirals

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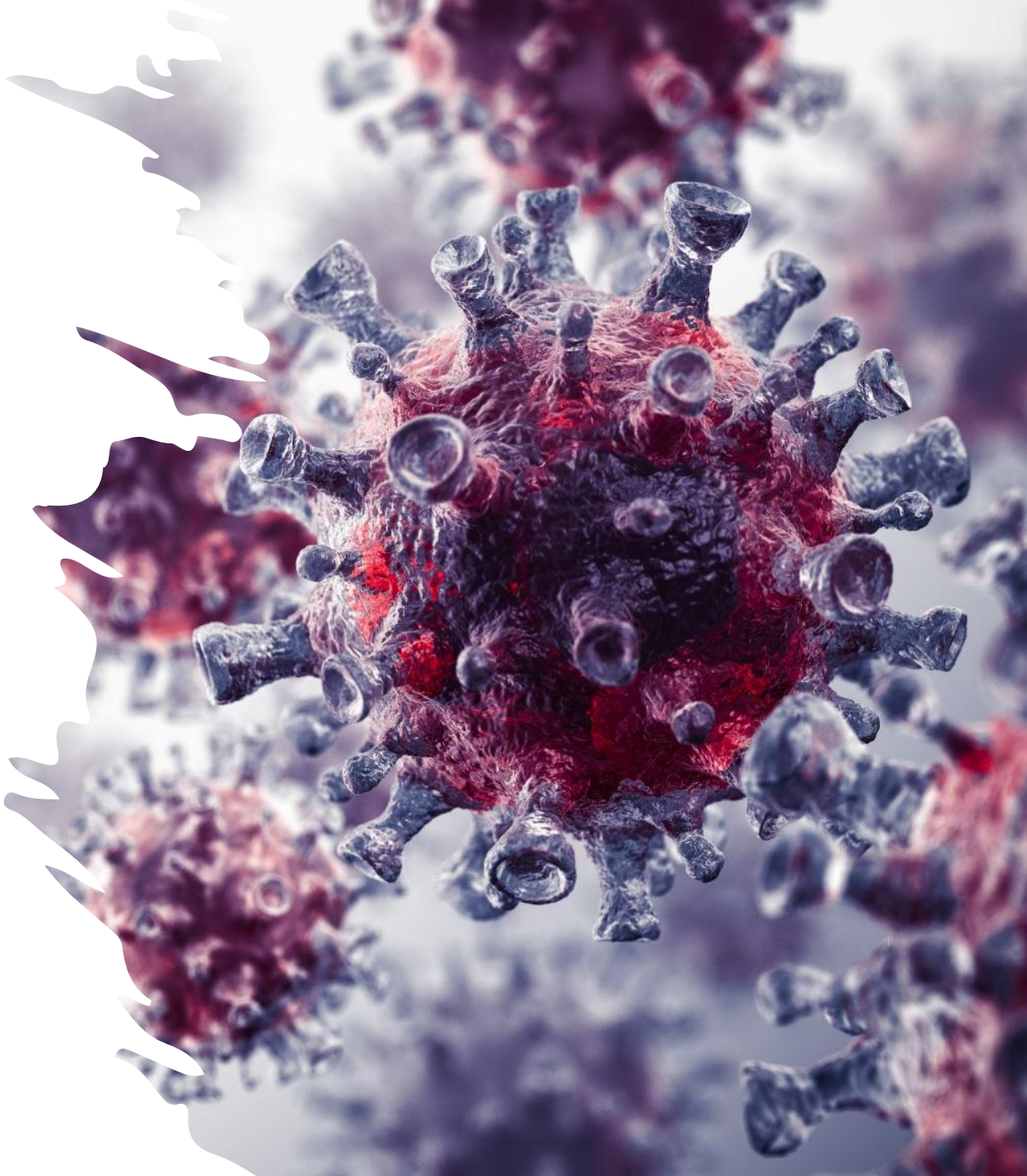
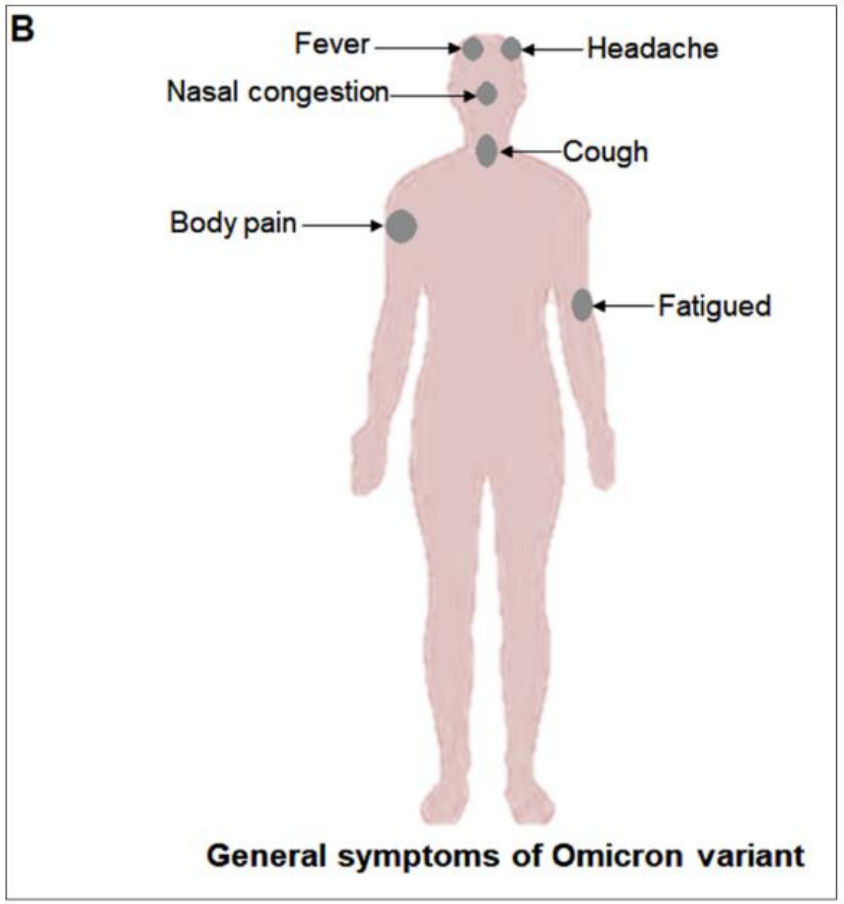
DIFFERENCE BETWEEN INFECTION AND DISEASE

- When a pathogen like a virus enters into the body of a host and multiply or replicate over there, causing harm to the host is called infection. An infection may cause **symptoms** and be **clinically visible** or they may cause **no symptoms and be subclinical**.
- When the condition of the body gets altered from normal and functional state of the organisms to the abnormal and dysfunctional state, associated with certain different kinds of signs and symptoms is called as **disease**.



Simptoms

- Mild simptoms are prevalent in Omicron variant infection
- The hospitalization rate in ICU is lower than the other variants
- Few patients needed oxygen support in comparison with the other variants



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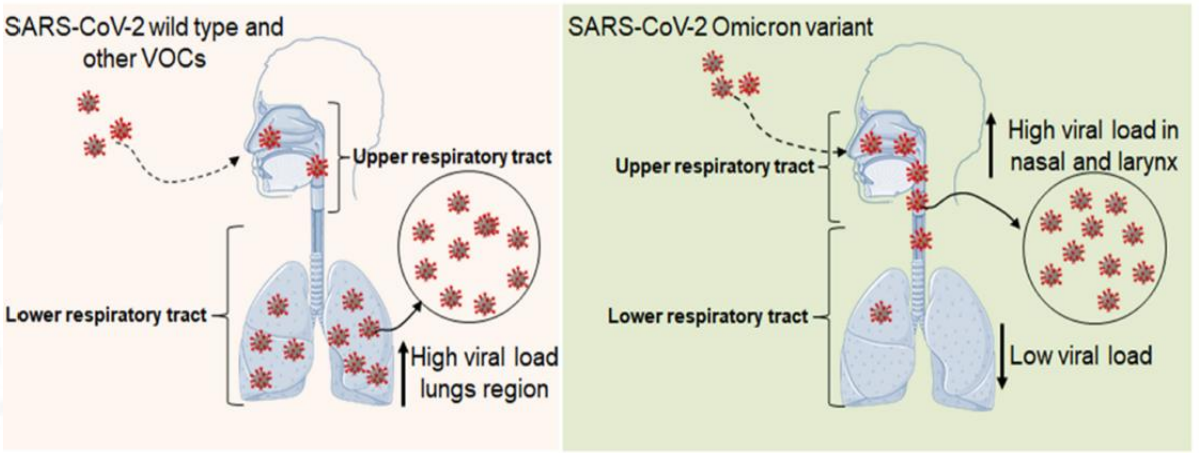
- The omicron virus is found in higher concentration in upper respiratory tract cells than lower ones.
- The motivation is the high affinity of the RBD to the ACE receptors of these cells
- It leads with simptoms as:

  rhinorrea, congestion, cough, sore throat, hoarse voice



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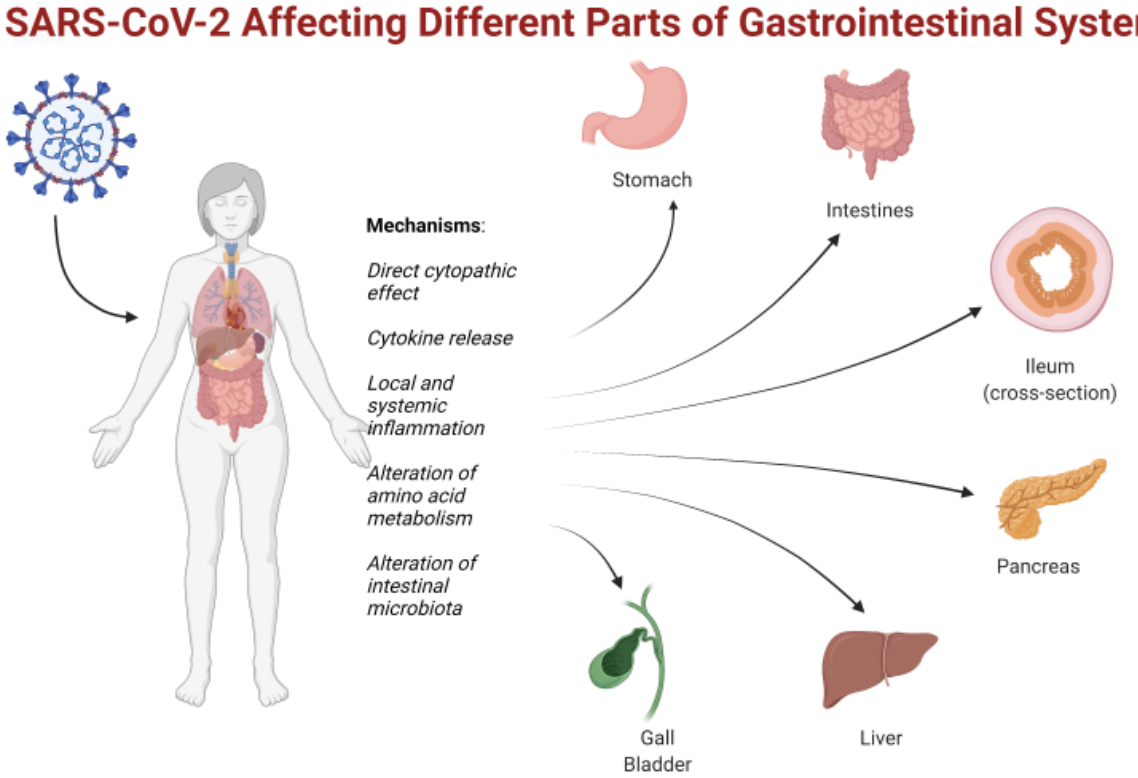
- The durations of the simptoms is lower in Omicron variant than the others (6,8 days vs 8,9 in Delta variants)
- Among the gastroenterological symptoms, vomiting is the most common one
- Diarrhea and abdominal cramps are common in children aged 5–9 years who are infected with Omicron.
- Gastrointestinal simptoms are present in almost 50% of infected population and in 10-25% persist for months
- These symptoms include heartburn, constipation, diarrhoea and abdominal pain and decline in prevalence with the passage of time.
- The pathophysiology of these symptoms is unknown but likely to be multifactorial



Impact of COVID-19 on the Gastrointestinal Tract: A Clinical Review

Haider Ghazanfar · Sameer Kandhi · Dongmin Shin · Aruna Muthumanickam · Hitesh Gurjar · Zaheer A. Qureshi · Mohammed Shaban · Mohamed Farag · Asim Haider · Pravash Budhathoki · Tanushree Bhatt · Ali Ghazanfar · Abhilasha Jyala · Harish Patel

Published: March 20, 2022 DOI: 10.7759/cureus.23333

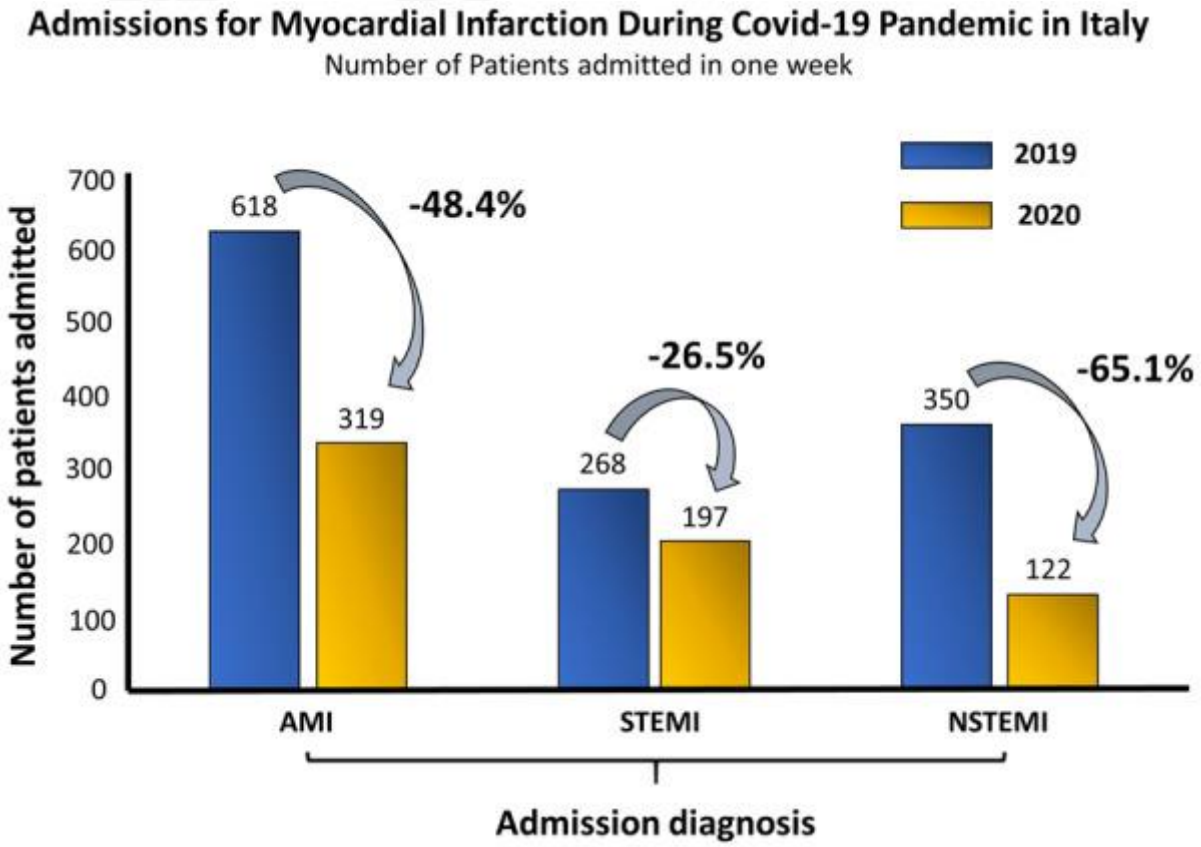
Increase of Acute cardiovascular event

Prothrombotic effect of the COVID-19

Multifactiorial effect of the infection above the cardiovascular system

Critical decrease of follow-up of chronic cardiovascular disease

People concerns about engaging with Hospitals and Health Care System



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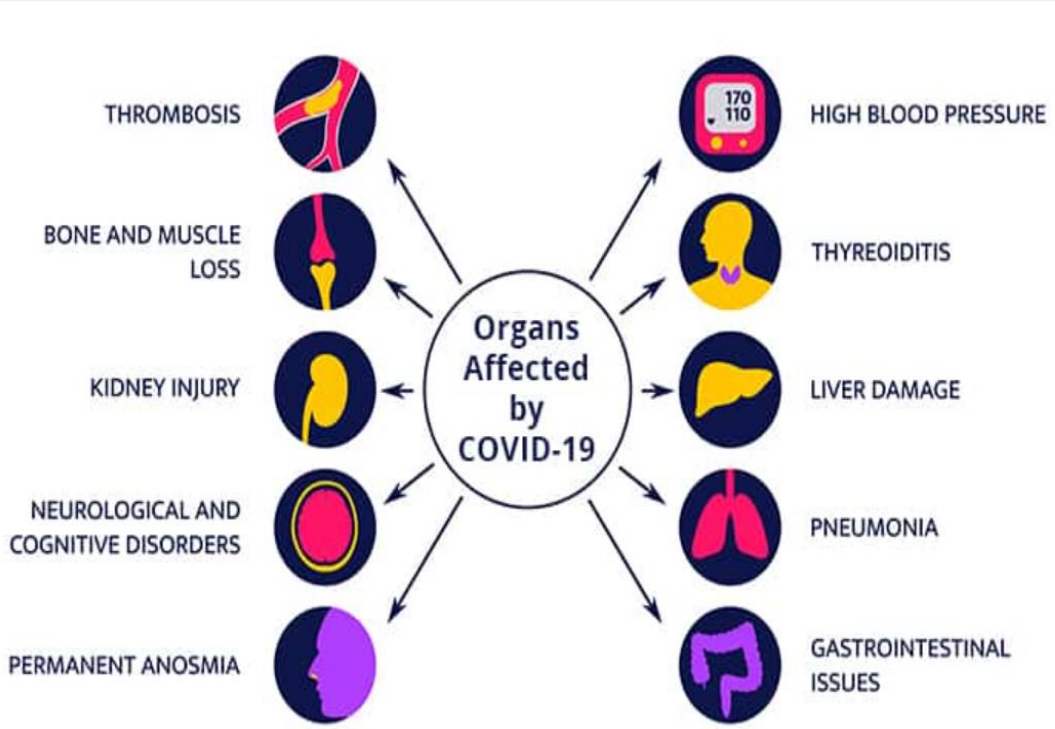
Not only lungs are affected by COVID-19



- Anosmia and ageusia are not peculiar simptoms of Omicron variant infection
- Neurological and cognitive disorders are related to direct and undirect damage of CNS
- Main simptoms are seizure, dizzines and headhache

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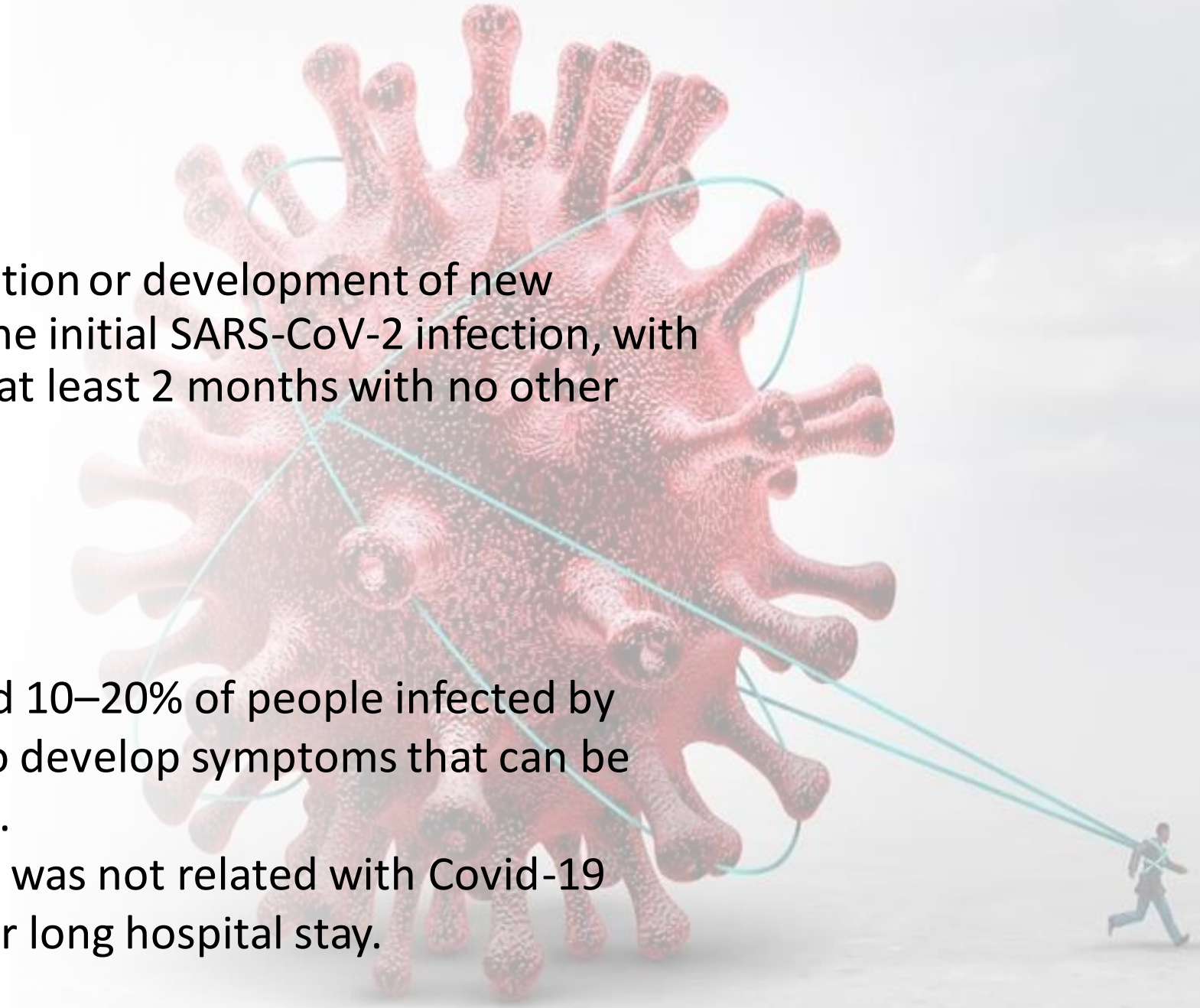
LONG COVID



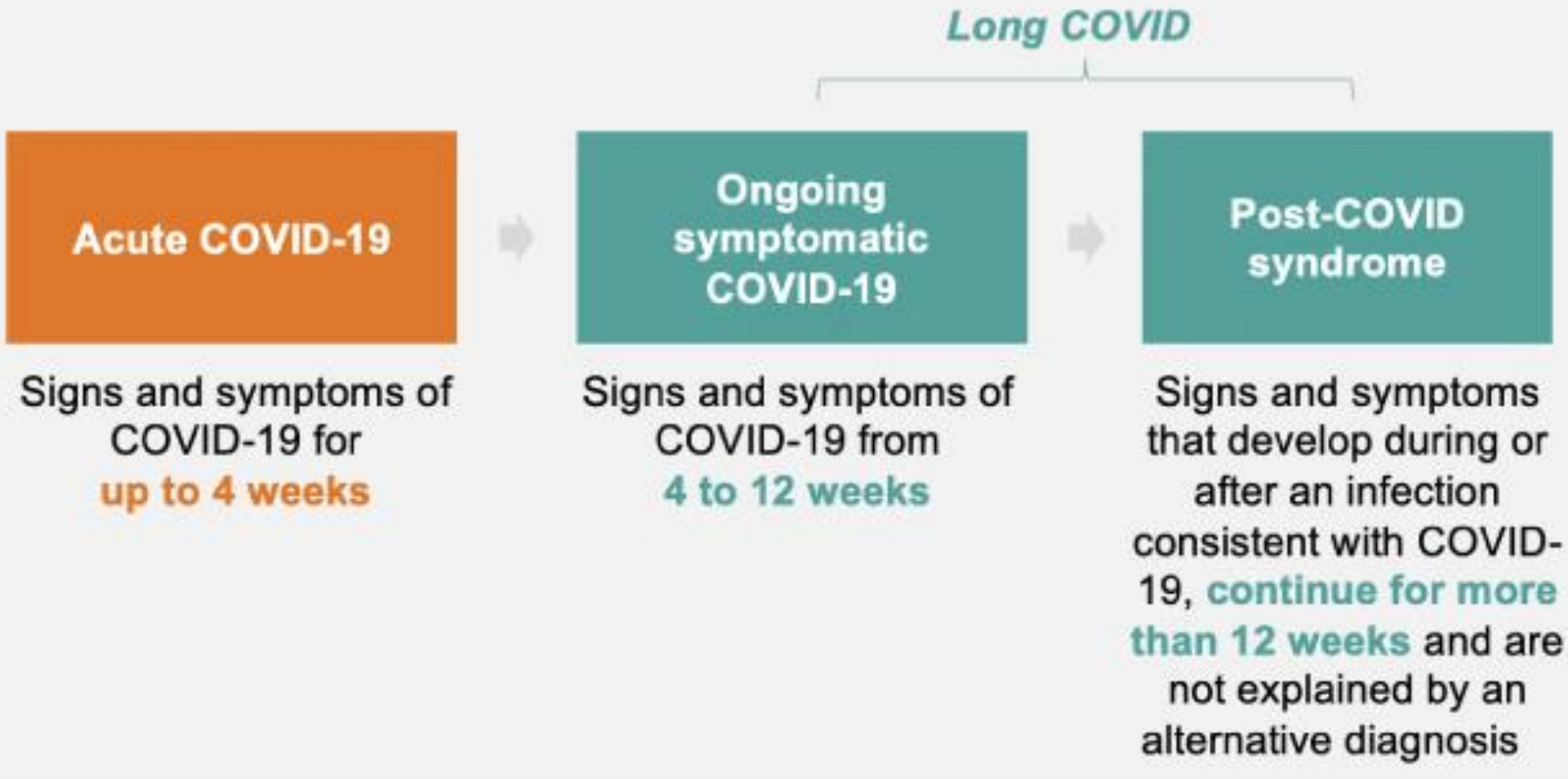
DEFINITION:

It is defined as the continuation or development of new symptoms 3 months after the initial SARS-CoV-2 infection, with these symptoms lasting for at least 2 months with no other explanation.

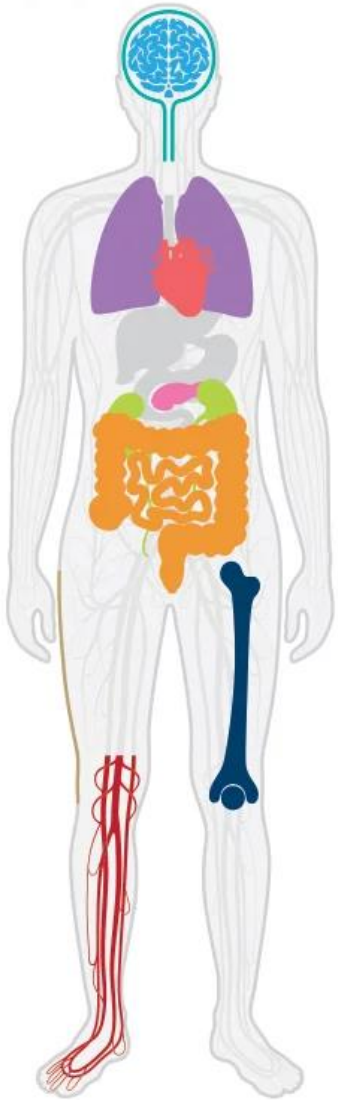
NUMBERS AFFECTED:

- Studies show that around 10–20% of people infected by SARS-CoV-2 may go on to develop symptoms that can be diagnosed as long COVID.
- Persistence of symptoms was not related with Covid-19 severity, ICU admission or long hospital stay.

Terminology and Definition of Long COVID



Reported symptoms after SARS-CoV-2 infection



Mental Health
- Anxiety
- Depression
- Sleep problems
- Substance abuse

Respiratory System
- Cough
- Low blood oxygen
- Shortness of breath

Kidney
- Acute kidney injury
- Chronic kidney disease

Gastrointestinal
- Diarrhea
- Acid reflux
- Constipation

Skin Disorders
- Rash
- Hair loss

Blood Disorders
- Anemia
- Blood clots

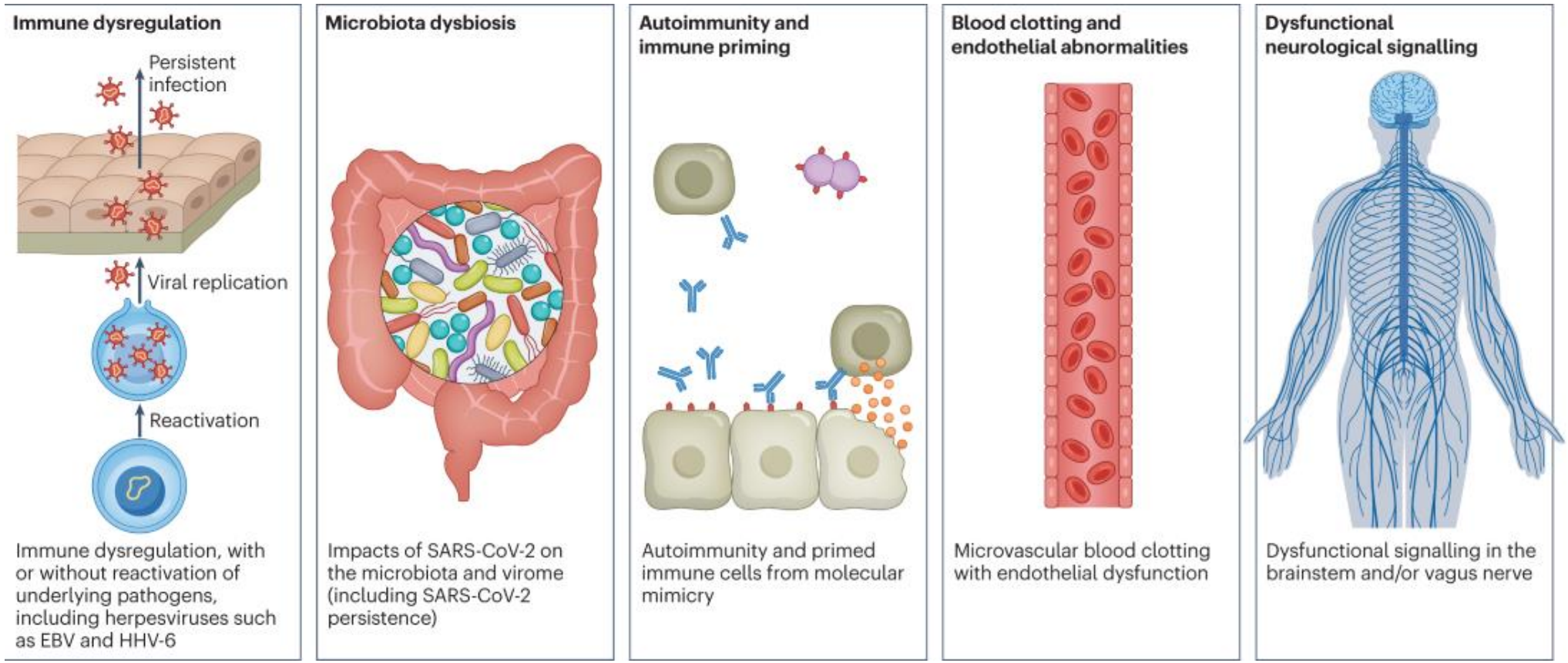
Nervous System
- Stroke
- Headaches
- Memory problems
- Loss of smell and taste

Cardiovascular
- Arrhythmia
- Palpitations
- Heart failure
- Acute coronary disease

Metabolic/Endocrine
- Obesity
- Diabetes
- High cholesterol

Musculoskeletal
- Joint pain
- Muscle weakness

General
- Fatigue
- Malaise
- Mitochondrial dysfunction


Immune dysregulation
Persistent infection
Viral replication
Reactivation
Immune dysregulation, with or without reactivation of underlying pathogens, including herpesviruses such as EBV and HHV-6
Microbiota dysbiosis
Impacts of SARS-CoV-2 on the microbiota and virome (including SARS-CoV-2 persistence)
Autoimmunity and immune priming
Autoimmunity and primed immune cells from molecular mimicry
Blood clotting and endothelial abnormalities
Microvascular blood clotting with endothelial dysfunction
Dysfunctional neurological signalling
Dysfunctional signalling in the brainstem and/or vagus nerve

Symptoms
Pathology

Heart

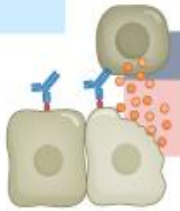
- Chest pain
- Palpitations

- Cardiac impairment
- Myocardial inflammation
- POTS

Lungs

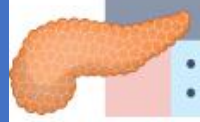
- Cough
- Dyspnoea

- Abnormal gas exchange



Immue system

- Autoimmunity
- MCAS



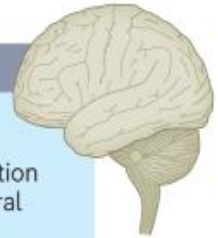
Pancreas

- Diabetes
- Pancreas injury

Gastrointestinal tract

- Abdominal pain
- Nausea

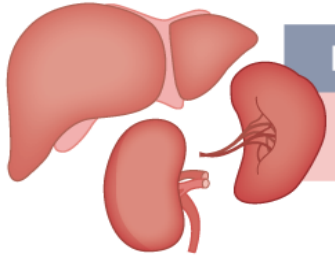
- Gut dysbiosis
- Viral persistence and viral reservoir



Neurological system

- Cognitive impairment
- Fatigue
- Disordered sleep
- Memory loss
- Tinnitus

- Dysautonomia
- ME/CFS
- Neuroinflammation
- Reduced cerebral blood flow
- Small fibre neuropathy



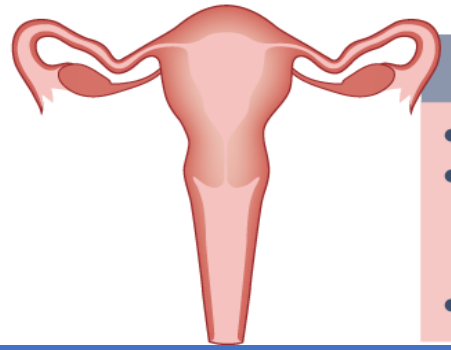
Kidneys, spleen and liver

- Organ injury

Blood vessels

- Fatigue

- Coagulopathy
- Deep vein thrombosis
- Endothelial dysfunction
- Microangiopathy
- Microclots
- Pulmonary embolism
- Stroke



Reproductive system

- Erectile dysfunction
- Increased severity and number of premenstrual symptoms
- Irregular menstruation

- Reduced sperm count

How can I prevent long COVID?

- The best way to avoid long COVID, is to avoid getting COVID in the first place, like from vaccination and masking.
- There is also evidence that vaccinated people who get COVID-19 are less likely to have post-COVID conditions.

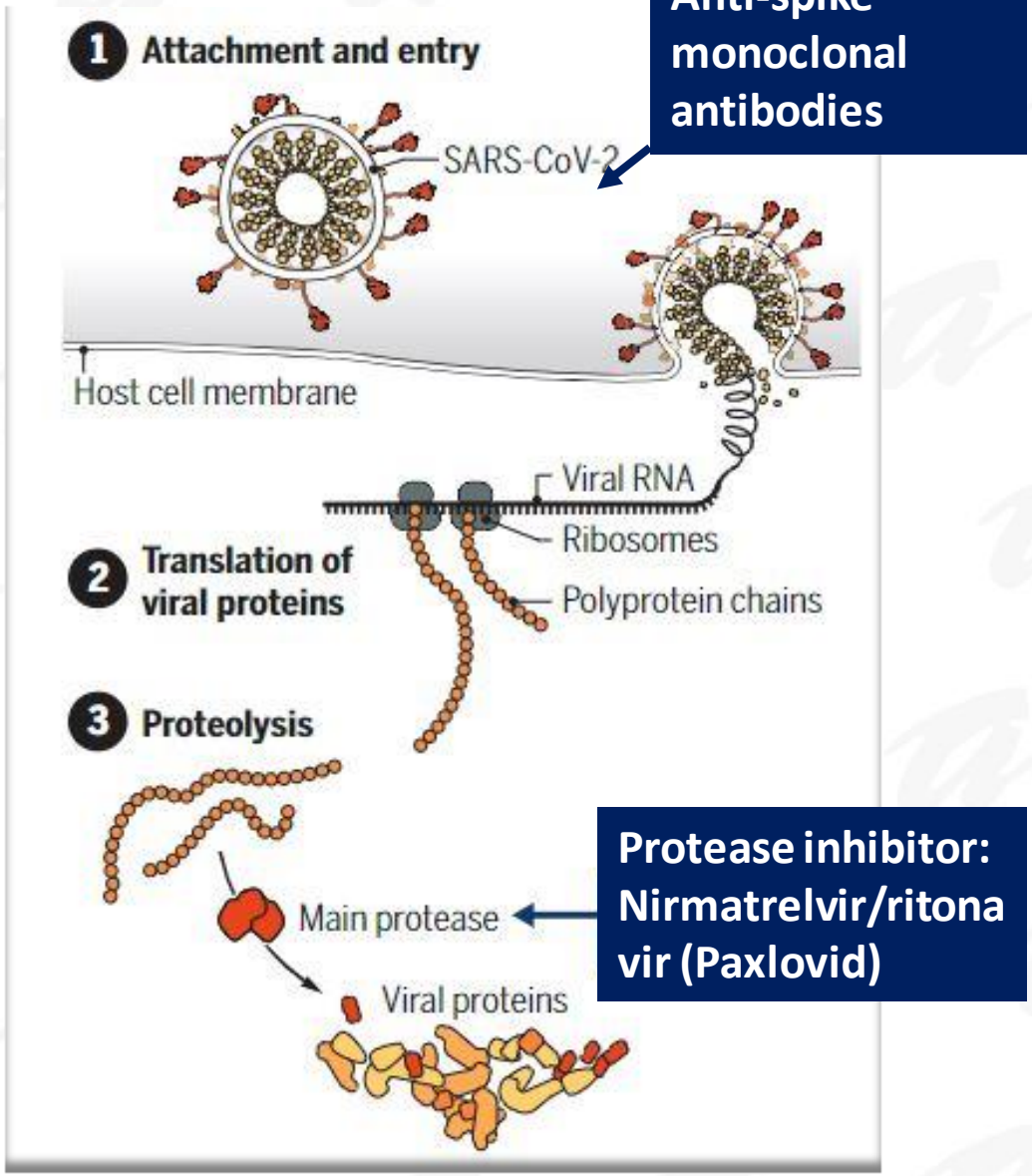
What are the treatment options?

- There is no specific cure for long COVID, but there may be treatments that can help you feel better depending in your syntoms.
- In many hospitals they build a team of health professionals to help people with long covid.

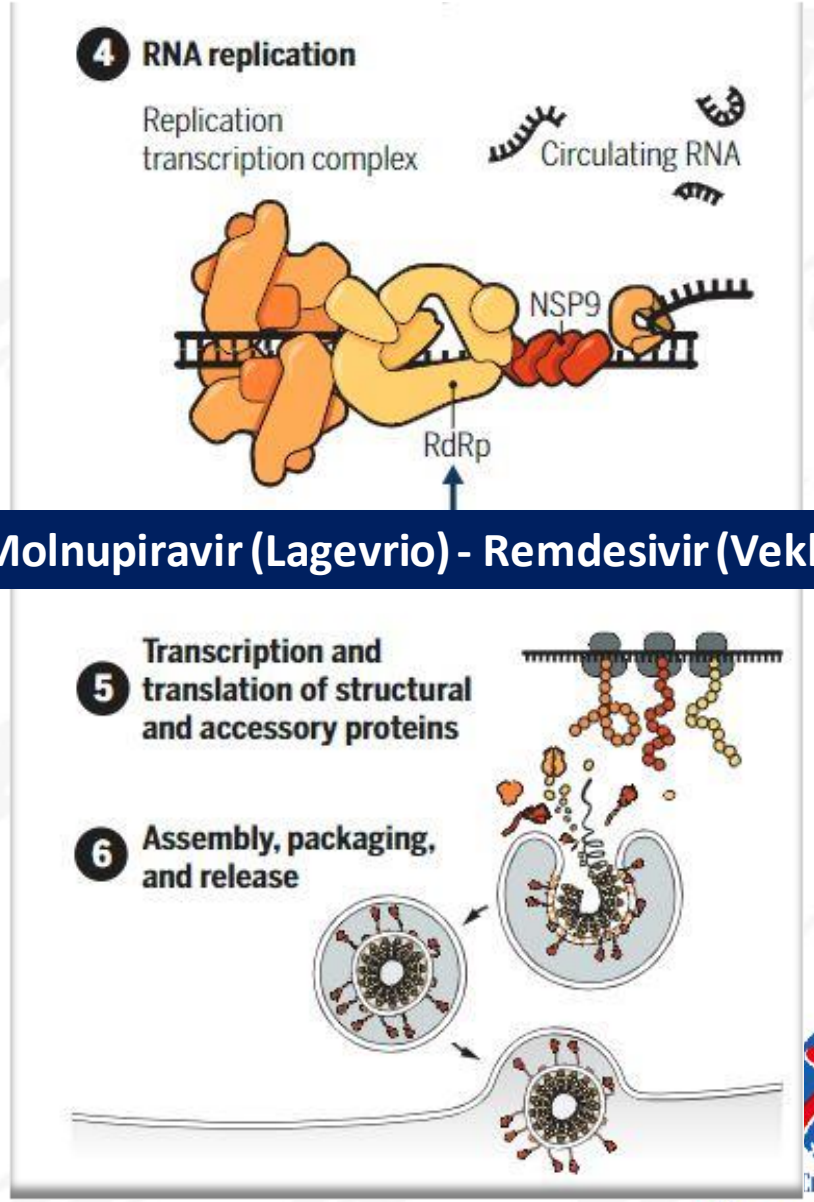
AUTHORISED DRUGS FOR COVID-19 IN EU

- Paxlovid
- Remdesivir
- Monlupinavir
- Anakinra
- Tocilizumab
- Regdamvimab
- Sotrovimab
- Casilinimab/Imdevimab
- Tixagevimab/tilgavimad

Anti-spike monoclonal antibodies



Protease inhibitor: Nirmatrelvir/ritonavir (Paxlovid)



Molnupiravir (Lagevrio) - Remdesivir (Veklury)

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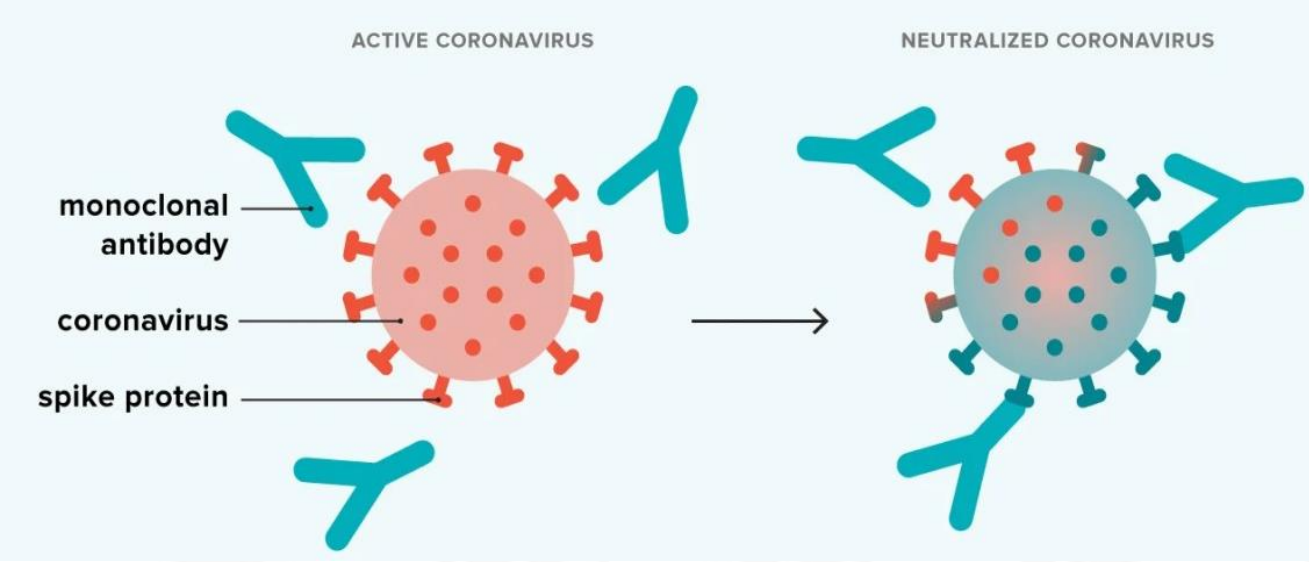
ANTI-SPIKE MONOCLONAL ANTIBODIES



Used in patients at increased risk of their COVID-19 disease becoming severe and who do not require supplemental oxygen.

Some monoclonal antibodies are also approved for preventing COVID-19.

Monoclonal antibodies attach to the spike proteins and prevent the virus entering others cells

Poorly effective at neutralizing most Omicron variants and do not significantly neutralise the variants which are dominant in the EU

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ANTIVIRALS

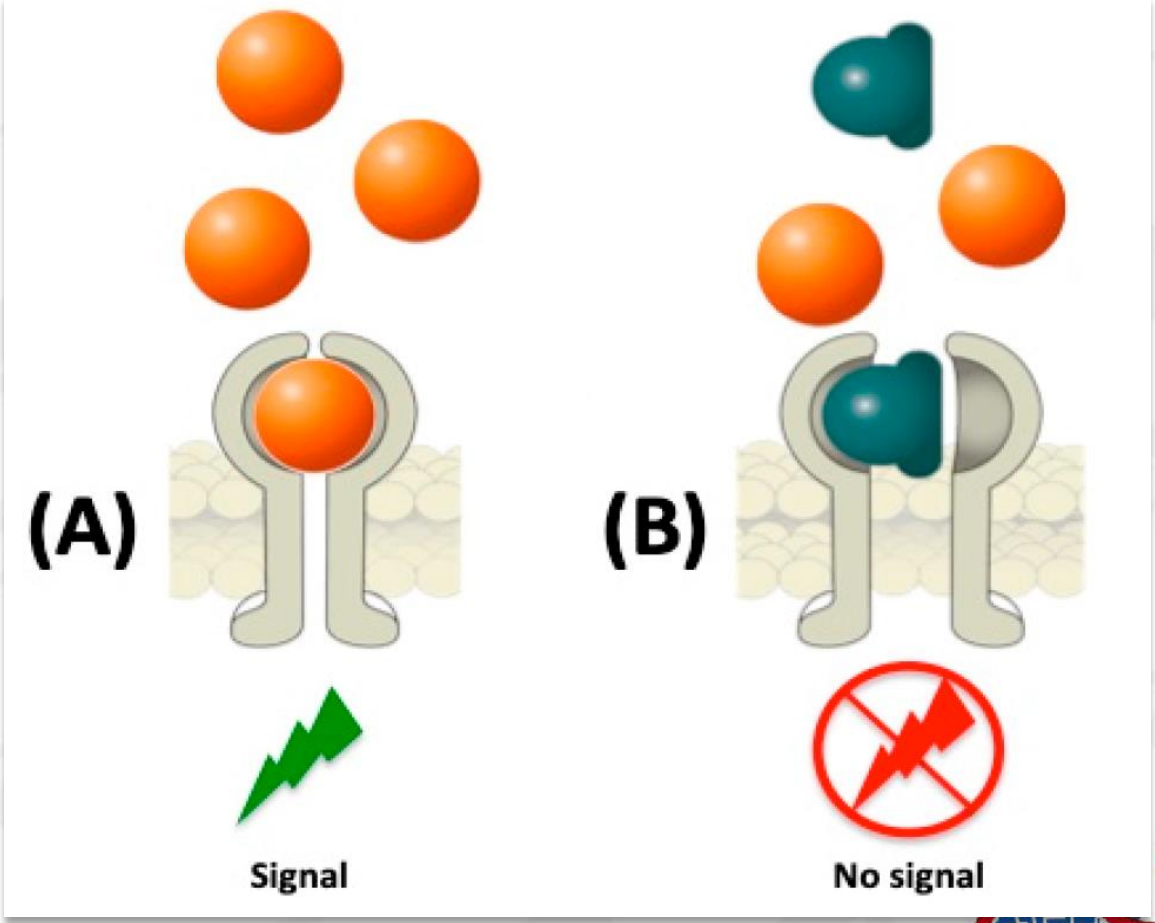
Based on the totality of data, it was not possible to conclude that Lagevrio can reduce the risk of hospitalisation or death or shorten the duration of illness or time to recovery in adults at risk of severe disease. Furthermore, it was not possible to identify a specific group of patients in whom a clinically relevant benefit of Lagevrio could be demonstrated.

Antivirals are a class of drug that inhibit viral replication

	PAXLOVID®	RENDESIVIR	MOLNUPINAVIR
Pros	•Highly efficacious •Oral regimen •Ritonavir studied (safe) in pregnancy	•Highly efficacious •Studied in pregnancy •Few/no drug interactions	•Or…men •Not…ave drug interac…
Cons	•Drug drug interactions	•Requires IV infusion on 3 consecutive days	•Low…ficacy •Concern: mutagenicity •Not recommended in pregnancy/children

IMMUNOMODULATORS

- **Anakinra** is a monoclonal antibody that blocks the interleukin IL-1.
  Guidelines in January 2023 found insufficient evidence to recommend for or against anakinra for the treatment of COVID-19.
- **Tocilizumab** is an IL-6 receptor monoclonal antibody
  Guidelines conditionally suggest the use of tocilizumab among hospitalized patients with progressive severe or critical COVID-19.



COTICOSTEROIDS

Can be use in SARS-CoV-2 infection among hospitalized patients with severe COVID-19 (defined as patients with SpO2 ≤94% on room air, or those who require either supplemental oxygen, mechanical ventilation or extracorporeal mechanical oxygenation)

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HYDROXYCHLOROQUINE/CHLOROQUINE

- Data from *in vitr* imental studies sho t hydroxychloroquine and chloroqui ibitory effec -2.
- RCTs did not f f a oxychloroquine for the treatment of hydroxycholoquine arm.

AZITHROMYC

The antibiotic azi has been postu ing antiviral and anti-inflammatory p nits and has been studie the treatment of COVID-19. However, multiple studies have not identified any clinical benefit

COVALESCENT PL MA

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  co cent plasma, no differenc
  observed in mortality or other clinical outcomes between the plasma and placebo groups.

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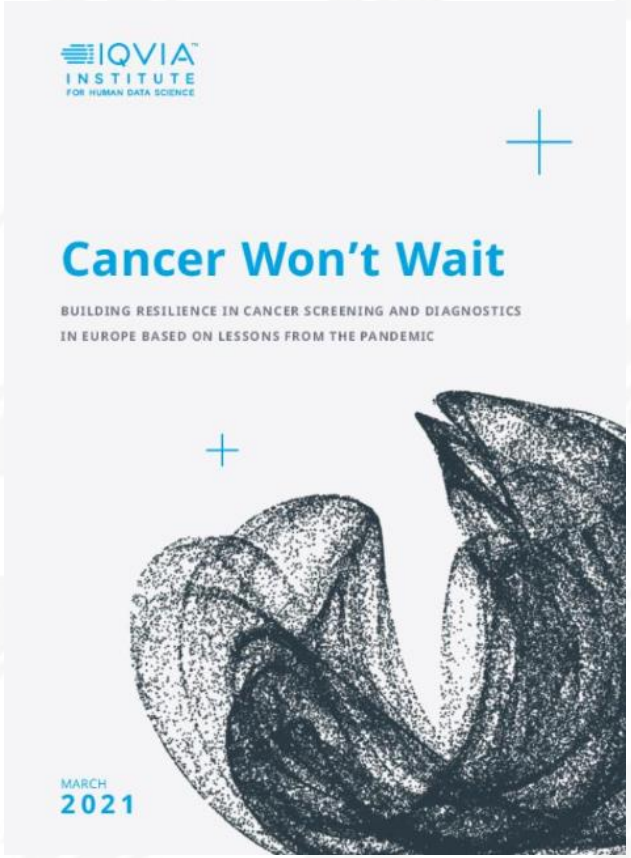
An estimated 100 million Cancer screening tests were not performed in Europe as a result of the pandemic

Colon-rectal cancer	• Occult blood in the stool
Breast cancer	• Mammography
Cervical cancer	• Pap-test

- Reduced screenings and testing can be attributed to both health system issues and patient concerns

- Re-prioritisation of health system resources has caused a reduction in capacity and significant disruption to the provision of health services

- Patient attitudes and concerns about engaging with the health system, especially **for asymptomatic conditions** and **preventative measures**, have also triggered the steep decline in screenings and testing



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At the beginning of the COVID-19 pandemic, a suspension of many nonurgent medical services was imposed all over the world.

Affected services concerned, for example, family planning and abortion[4]; HIV prevention, testing, and care, and cancer prevention

On April 2020 we registered the lowest peak of cancer screenings provided with a reduction near to 70% in comparison with the previous period

The average of lost screening is 45%

It suppose to be the cause of a raise of cancer mortality for delayed diagnosis and therapies

Analisys conducted on data from North and South America, Europe on January to October 2020

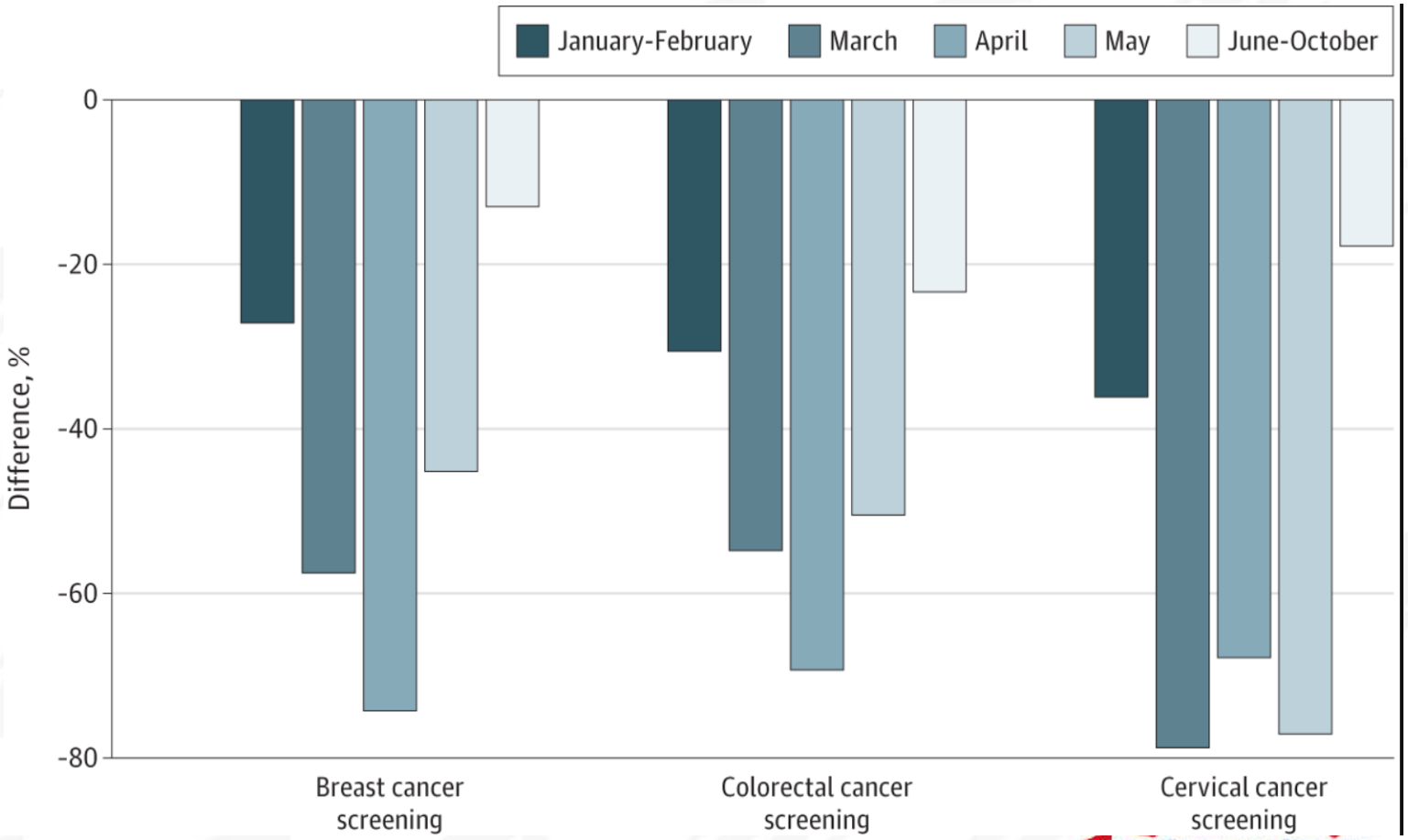

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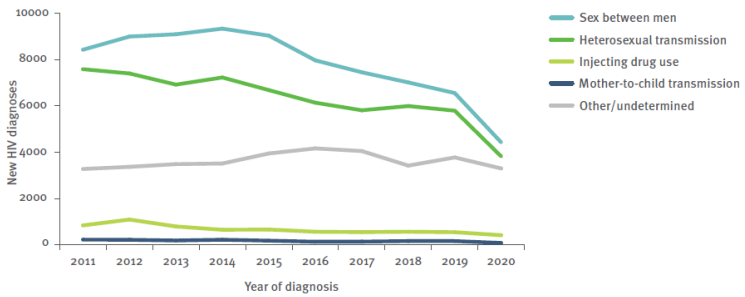
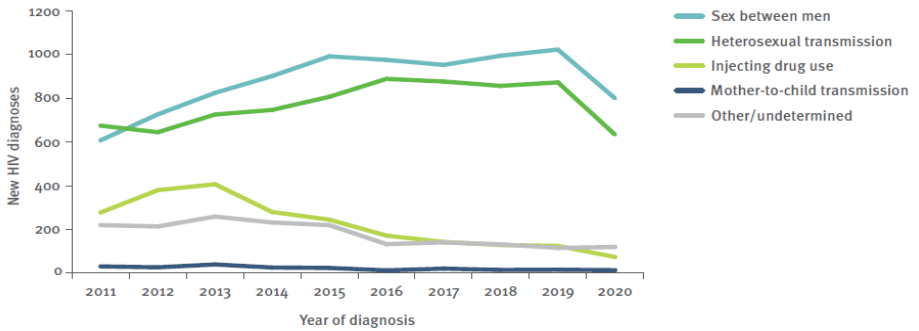
Figure 2.18: New HIV diagnoses, by transmission mode and year of diagnosis, West, 2011–2020



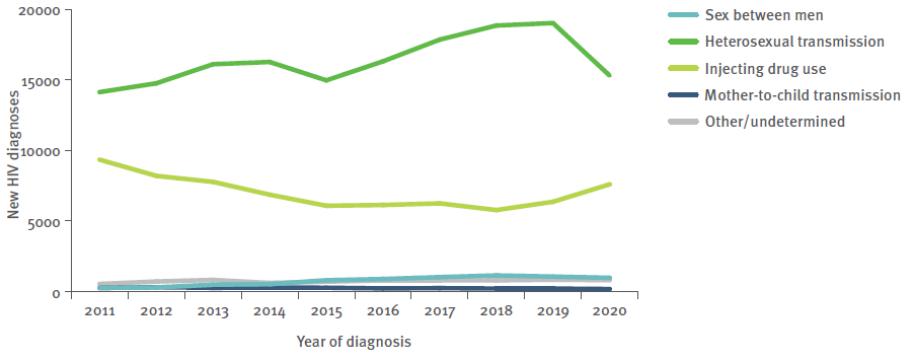
Data from Andorra, Monaco and Portugal excluded due to inconsistent reporting during the period; data from Iceland, Ireland and Malta excluded due to incomplete reporting on transmission mode during the period; data from Italy and Spain excluded due to increasing coverage of national surveillance during the period.

Figure 2.16: New HIV diagnoses, by transmission mode and year of diagnosis, Centre, 2011–2020



Data from Bosnia and Herzegovina, North Macedonia,Poland and Turkey excluded due to incomplete reporting on transmission mode during the perio

Arithmetic scale



The number of **new HIV infection** diagnosis on average has been reduced from 2020 all over European countries. Because of the health care system measure adopted to face the COVID-19 pandemia the number of test provided has been strictly reduced

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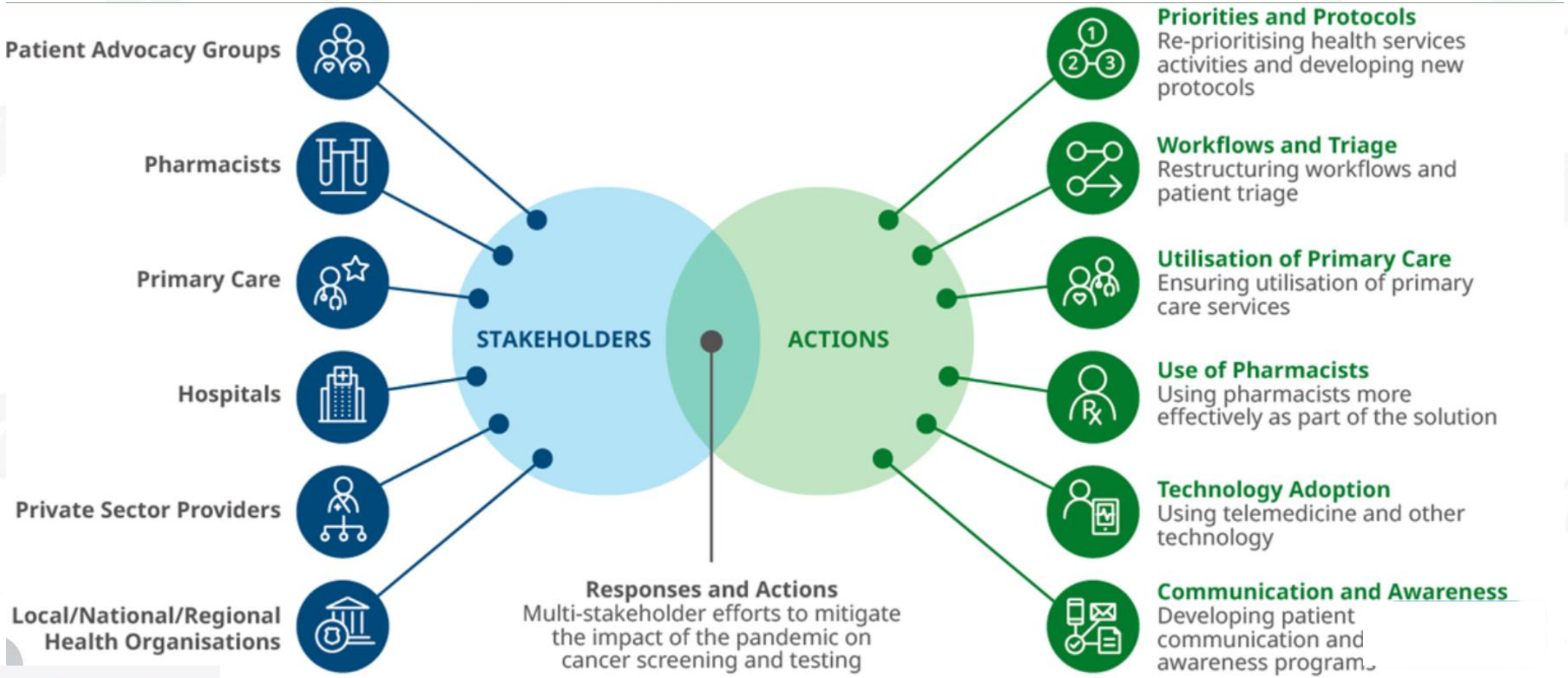

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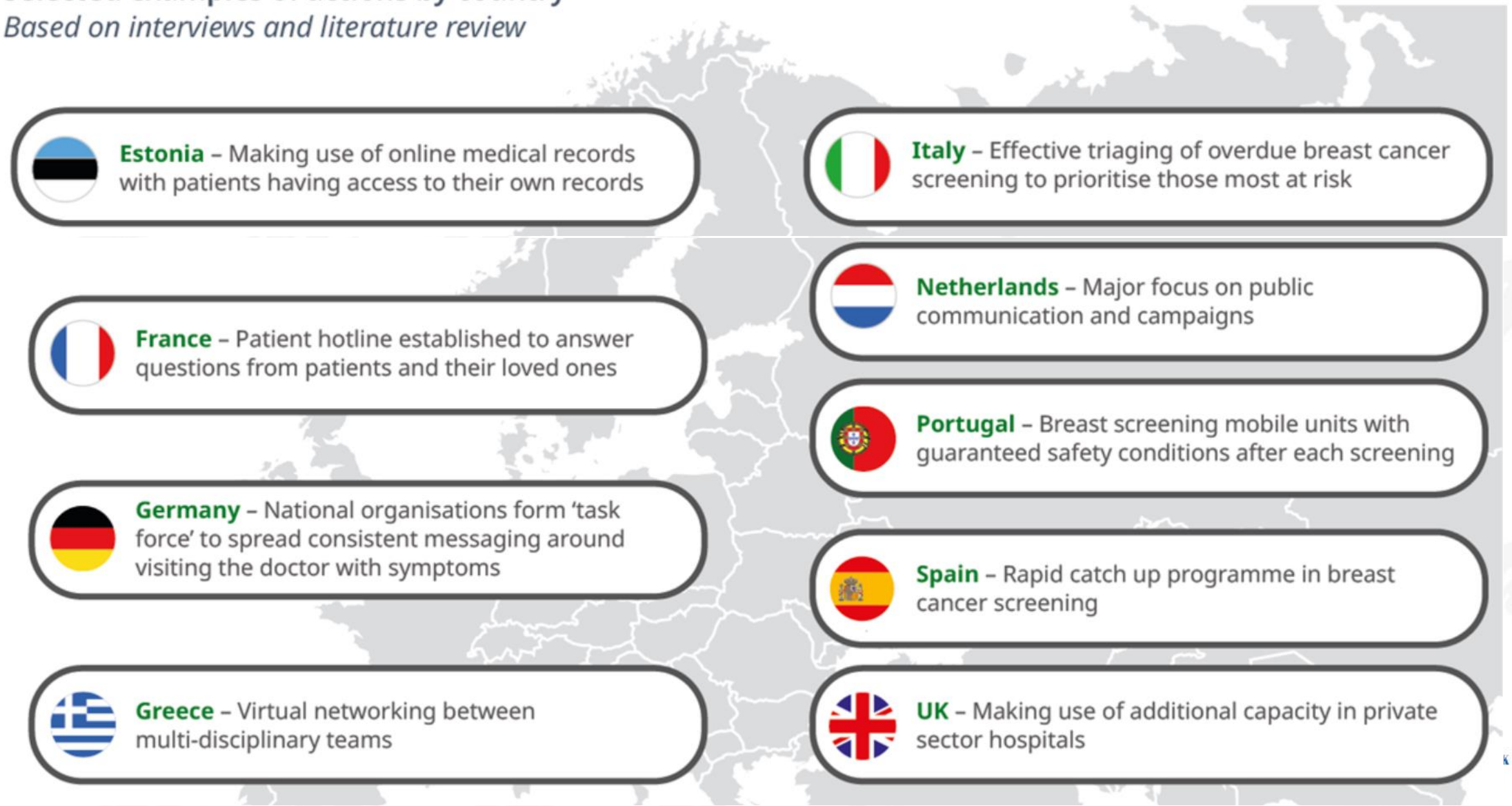
Selected examples of actions by country

Based on interviews and literature review



Estonia – Making use of online medical records with patients having access to their own records

France – Patient hotline established to answer questions from patients and their loved ones

Germany – National organisations form 'task force' to spread consistent messaging around visiting the doctor with symptoms

Greece – Virtual networking between multi-disciplinary teams

Italy – Effective triaging of overdue breast cancer screening to prioritise those most at risk

Netherlands – Major focus on public communication and campaigns

Portugal – Breast screening mobile units with guaranteed safety conditions after each screening

Spain – Rapid catch up programme in breast cancer screening

UK – Making use of additional capacity in private sector hospitals

- Ghazanfar H, Kandhi S, Shin D, et al. (March 20, 2022) Impact of COVID-19 on the Gastrointestinal Tract: A Clinical Review. Cureus 14(3): e23333. doi:10.7759/cureus.23333
- **The nervous system during COVID-19: Caught in the crossfire** Nick R. Natale, John R. Lukens, William A. Petri Jr First published: 30 June 2022
- IQVIA institute- Cancer won't wait- 2021
- **Global Association of COVID-19 Pandemic Measures With Cancer Screening** A Systematic Review and Meta-analysis

. 2020 Jun 7;41(22):2083-2088.
doi: 10.1093/eurheartj/ehaa409.
Reduction of hospitalizations for myocardial infarction in Italy in the COVID-19 era

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