COVID-19 in Europe - the rocky road to recovery

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Epidemiology

- In December 2019, China reported the first cases of the coronavirus disease 2019 (COVID-19).
- This disease, caused by the severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2), has developed into a pandemic.
- **Situation update 20 August 2020, dataset collected 6:00-10:00 CET**

22 431 929 cases	Worldwide	787 773 deaths	Whereof 180 231 deaths in the EU/EEA and UK	1 981 994 cases	In the EU/EEA and the UK

- Unequivocally, the COVID-19 pandemic is the gravest health and socio-economic crisis of our time

28.8.2020, 8 Uhr	Neu	Total seit Beginn der Epidemie
Laborbestätigte Infektionen	340	41 346
Hospitalisierungen	9	4527
Todesfälle	1	1725
Covid-19-Test	12 820	988 383

Mode of transmission

- Bats are considered natural hosts of these viruses yet several other species of animals are also known to act as sources. COVID 19 is closely related genetically to the SARS-CoV-1 virus
- The virus spread is now from person to person (human-to-human transmission). On average, one infected person will infect between two and three other people.

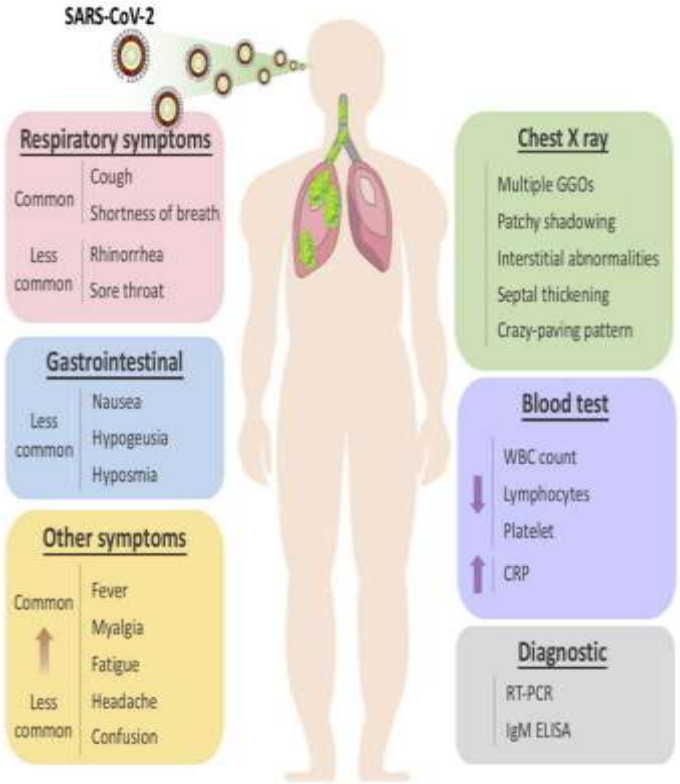
- The virus seems to be transmitted mainly via small respiratory droplets through sneezing, coughing, or when people interact with each other for some time in close proximity (usually less than one meter).
- These droplets can then be inhaled, or they can land on surfaces that others may come into contact with, who can then get infected when they touch their nose, mouth or eyes.
- The virus can survive on different surfaces from several hours (copper, cardboard) up to a few days (plastic and stainless steel). However, the amount of viable virus declines over time and may not always be present in sufficient numbers to cause infection.

- The incubation period for COVID-19 is currently estimated to be between one and 14 days.

Infectivity in Europe

- The infectious period may begin one to two days before symptoms appear, but people are likely most infectious during the symptomatic period, even if symptoms are mild and very non-specific
- The infectious period is now estimated to last for 7-12 days in moderate cases and up to two weeks on average in severe cases.
- Data from the EU show that around 20-30% of diagnosed COVID-19 cases are hospitalized and 4% have severe illness
- Hospitalization rates are higher for those aged 60 years and above, and for those with other underlying health conditions
- Elderly people above 70 years of age and those with underlying health conditions (e.g. hypertension, diabetes, cardiovascular disease, chronic respiratory disease and cancer) are considered to be more at risk of developing severe symptoms. Men in these groups also appear to be at a slightly higher risk than females.

Symptoms are Universal



Symptoms of COVID-19 vary in severity from having no symptoms at all (being asymptomatic) to having fever, cough, sore throat, general weakness and fatigue and muscular pain

In the most severe cases, severe pneumonia, acute respiratory distress syndrome, sepsis and septic shock, all potentially leading to death

Reports show that clinical deterioration can occur rapidly, often during the second week of disease

Recently, anosmia and in some cases the loss of the sense of taste have been reported as a symptom of a COVID-19 infection. There is already evidence from South Korea, China and Italy that patients with confirmed SARS-CoV-2 infection have developed anosmia/hyposmia, in some cases in the absence of any other symptoms.

Reality Check

Coronavirus: Why are international comparisons difficult?

Top Stories

Black Panther star Chadwick

Comparisons are difficult

So, is anything useful likely to emerge from all these comparisons?

"What you want to know is why one country might be doing better than another, and what you can learn from that," says Prof Jason Oke from the University of Oxford.

"And testing seems to be the most obvious example so far."

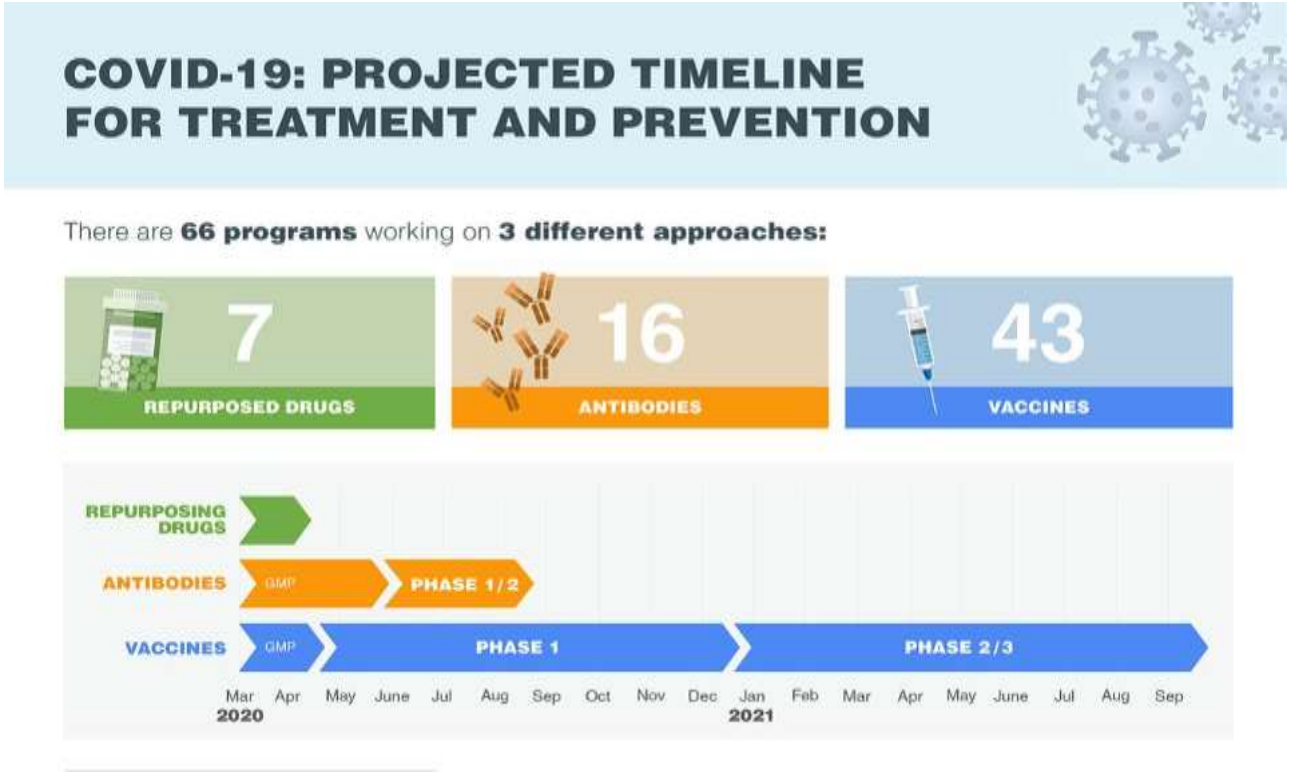
But until this outbreak is over it won't be possible to know for sure which countries have dealt with the virus better.

"That's when we can really learn the lessons for next time," says Prof Oke.

Therapy

- There is no specific treatment or vaccine for this disease.
- Healthcare providers are mostly using a symptomatic approach, meaning they treat the symptoms rather than target the virus, and provide supportive care (e.g. oxygen therapy, fluid management) for infected persons, which can be highly effective.
- In severe and critically ill patients, a number of drugs are being tried to target the virus, but the use of these need to be more carefully assessed in RCTs. Several clinical trials are ongoing to assess their effectiveness.
- As this is a new virus, no vaccine is currently available.
- Although work on a vaccine has already started by several research groups and pharmaceutical companies worldwide, it may be many months or even more than a year before a vaccine has been tested and is ready for use in humans.

Therapy


COVID-19: PROJECTED TIMELINE
FOR TREATMENT AND PREVENTION
There are 66 programs working on 3 different approaches:
7
REPURPOSED DRUGS
16
ANTIBODIES
43
VACCINES
REPURPOSING DRUGS
ANTIBODIES
GMP
PHASE 1/2
VACCINES
GMP
PHASE 1
PHASE 2/3
Mar Apr May June Jul Aug Sep Oct Nov Dec Jan Feb Mar Apr May June Jul Aug Sep
2020
2021

Therapy: repurposed drugs

- Remdesivir (GS-5734) is by far the most promising drug that exhibits broad-spectrum antiviral activities against RNA viruses
- It is a prodrug, whose structure resembles adenosine. Therefore, it can incorporate into nascent viral RNA, and further inhibit the RNA-dependent RNA polymerase
- This results in premature termination of the viral RNA chain and consequently halts the replication of the viral genome
- Remdesivir was originally developed against the Ebola virus. It proved its safety for humans, which allowed it to enter clinical trials immediately in the conditions of COVID-19 emergency.
- Importantly, it has been previously shown to exhibit antiviral activities against different coronaviruses, including SARS-CoV and MERS-CoV, in vitro and in vivo. In a recent in vitro study, remdesivir was also shown to inhibit SARS-CoV-2 (Tu et al. 2020).

DG Alerts COVID-19

According to data from an open-label Phase III study published in the *Journal of the American Medical Association*, patients with moderate coronavirus disease 2019 (COVID-19) pneumonia randomized to receive remdesivir treatment for up to 5 days had significantly higher odds of achieving clinical improvement at the 11-day mark than those receiving standard care.

However, the authors led by Christoph D. Spinner, MD, Technical University of Munich, School of Medicine, University Hospital Rechts der Isar, Munich, Germany, cautioned that the effect size was "of uncertain clinical importance." Meanwhile, patients randomized to a 10-day course of remdesivir did not have a statistically significant difference in clinical status compared to standard care at 11 days.

The study included nearly 600 hospitalized patients with confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and moderate COVID-19 pneumonia, with confirmed infiltrates by radiology, but with room-air oxygen saturations greater than 94% at rest. Participants were enrolled from March 15 through April 18, 2020, at 105 hospitals in the US, Europe and Asia. Median age was 57 years [interquartile range, 46-66]; 227 [39%] were women; 56% had cardiovascular disease, 42% hypertension, and 40% diabetes, and 533 (91%) completed the trial.

Therapy: Antibodies

- Monoclonal or polyclonal antibodies have been suggested as prophylactic and therapeutic tools (targeting hemagglutinin binding) against some viral infections, such as influenza
- Current efforts in developing monoclonal and polyclonal antibodies against coronaviruses mainly target MERS-CoV
- Numerous in vitro studies have shown that the spike protein of SARS-CoV is important in mediating viral entry into target cells. Furthermore, the cleavage and subsequent activation of the SARS-CoV spike protein by a protease of the host cell is absolutely essential for infectious viral entry.
- Type II transmembrane serine protease TMPRSS2 was suggested to be an important host protease that cleaves and activates the SARS-CoV spike protein in cell cultures, and was thus explored as a potential antiviral agent
- Use of stem cells against COVID-19 has been under evaluation in China recently
- Additionally, tocilizumab (Roche Pharmaceuticals, Basel, Switzerland) is a monoclonal antibody that is used in the treatment of RA exacerbation. It was designed to inhibit the binding of interleukin-6 to its receptors, thus alleviating cytokine release syndrome. Currently, it is also being investigated for treatment of COVID-19 (Jean et al. 2020)

Therapy: Vaccines

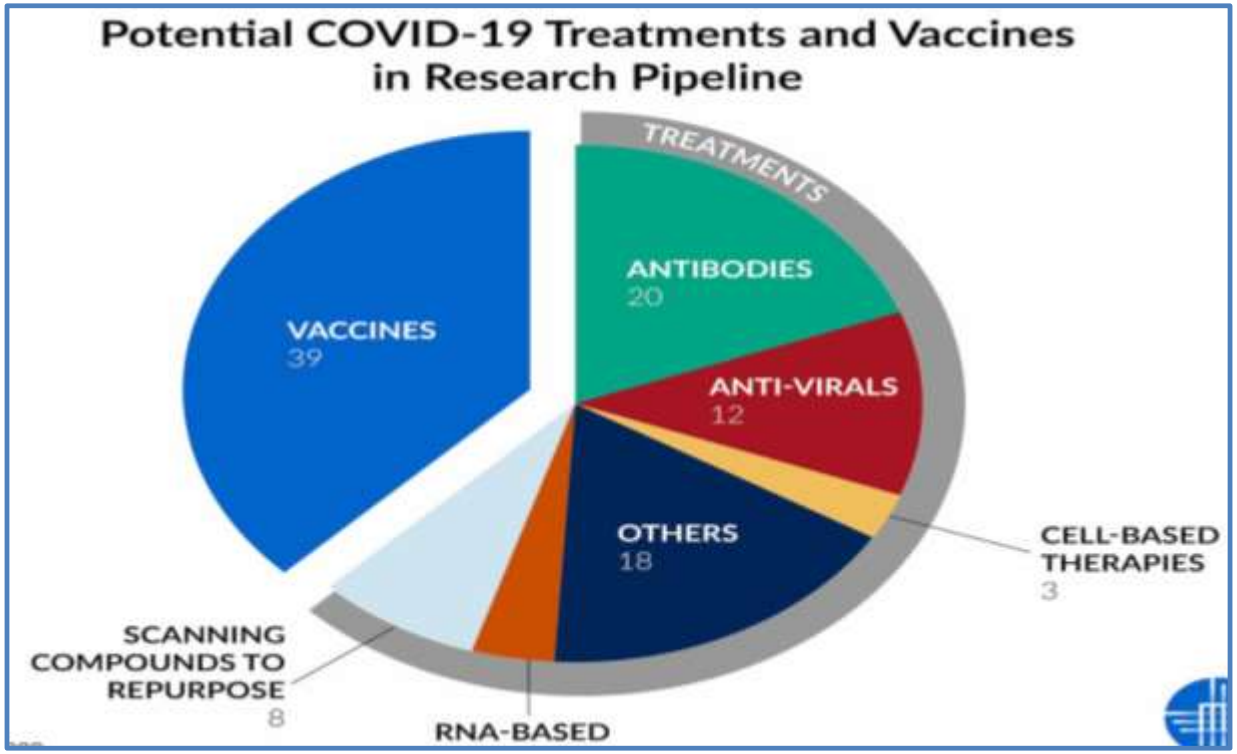
- Multiple strategies are adopted in the development of CoV vaccines; most of these target the surface-exposed spike (S) glycoprotein or S protein as the major inducer of neutralizing antibodies
- Several S-protein-based strategies have been attempted for developing CoV vaccines, e.g., use of full-length S protein or S1-receptor-binding domain (RBD) and expression in virus-like particles (VLP), DNA, or viral vector
- S protein is considered a key viral antigen for developing CoV vaccines, as shown in several preclinical studies.
- Although research is in progress to improve prevention, treatment, and control of COVID-19, the documented clinical data on different therapeutic approaches for CoVs are scarce
- Further research should be directed toward the study of SARS-CoV-2 in suitable animal models for analyzing replication, transmission, and pathogenesis
- Today there are no effective vaccines or specific antiviral drugs for COVID-19 (Dhama et al. 2020)

14:45 CET, 27 August 2020

UK awards £4M to two early stage COVID-19 vaccine projects

The UK government is backing two more coronavirus vaccine projects, with £4 million in grants for clinical trials awarded to the biotech companies Vaccitech and Scancell. Vaccitech has preclinical data showing its vaccine induces antibody and cell-mediated immune responses, and could be used as a standalone product or as a booster for first generation COVID-19 vaccines. Meanwhile Scancell is developing a DNA vaccine using technology that has been applied to cancer vaccines and which it has shown is safe, cost-effective and scalable. The product targets dendritic cells to stimulate T cells that identify and destroy infected cells.

Therapy: potential treatments



Current situation in Europe

The absence of an effective treatment or a vaccine combined with an exponential growth in infections from late February led many countries in Europe to implement non-pharmaceutical interventions such as “stay-at-home” policies (recommended or enforced), jointly with other community and physical distancing measures such as the cancellation of mass gatherings, closure of educational institutions and public spaces

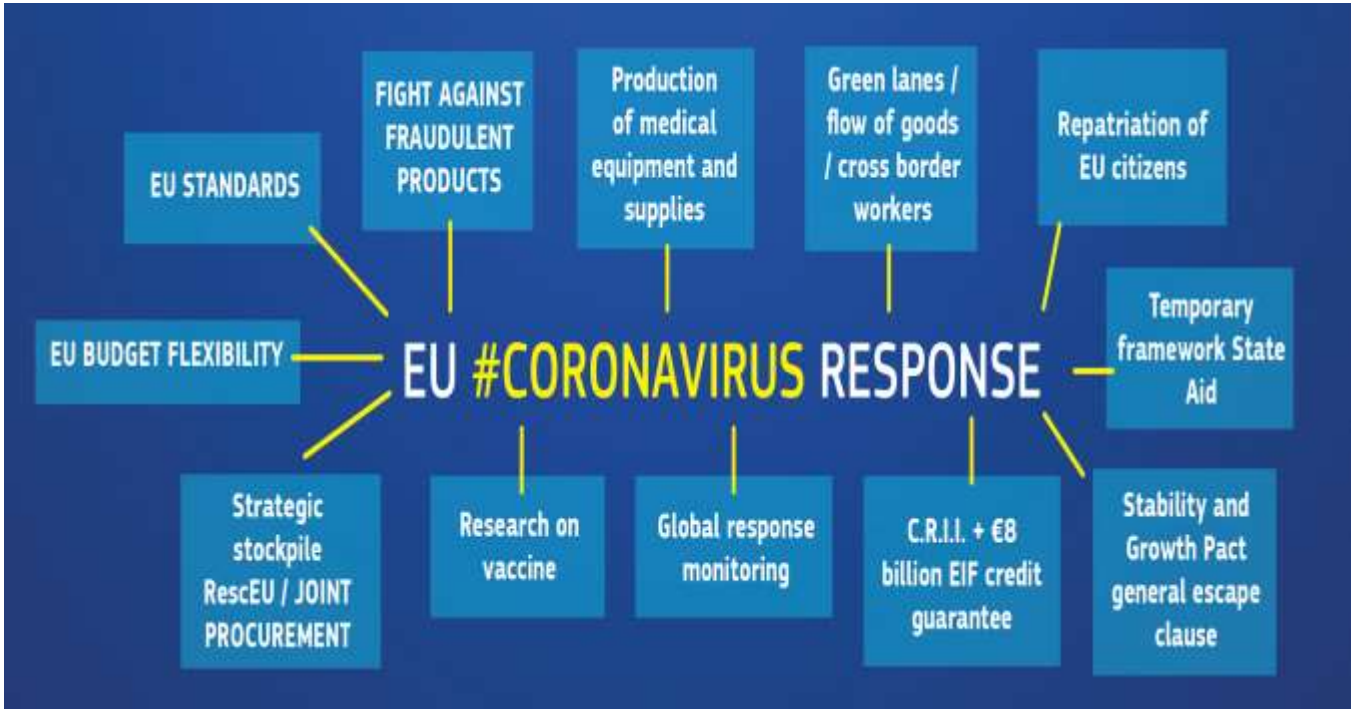
The rapid escalation of cases has placed enormous pressure on healthcare systems, and presented a major challenge for local services

To inform the European Commission and the public health authorities in Member States of the ongoing situation, ECDC publishes daily updates and continuously assesses the risk for EU citizens

ECDC and WHO develop technical guidance to support countries in their response

The European Commission is ensuring the coordination of risk management activities at EU level.

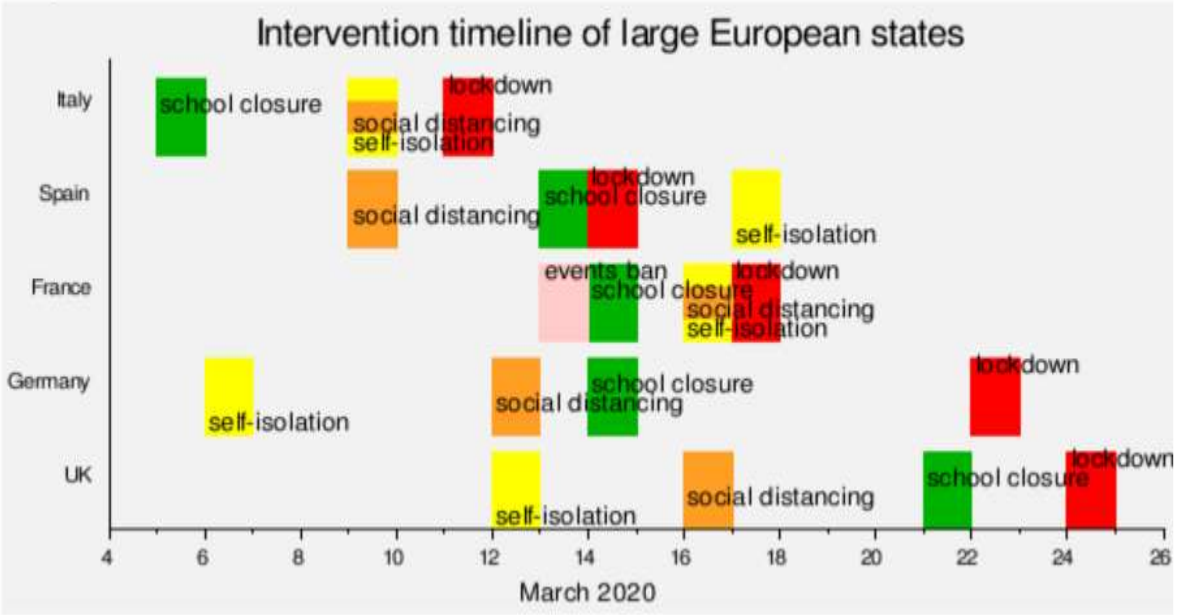
EU Coronavirus Response



COVID 19 Prevention

Response and criticism [edit]

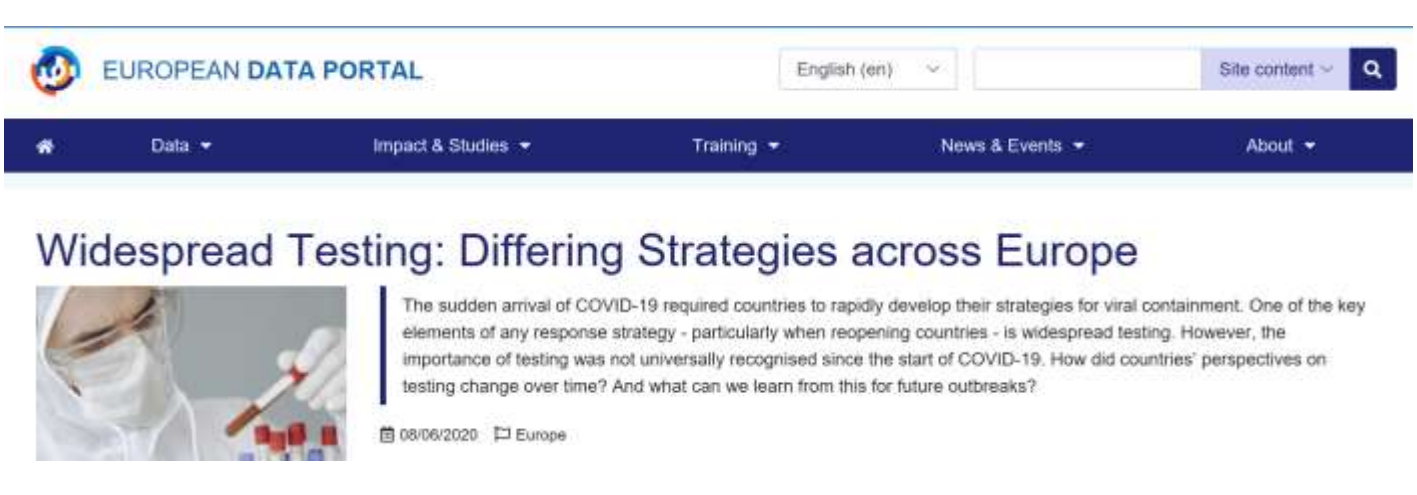
Timeline of interventions [edit]



EU solidarity [edit]

Main article: European Union response to the COVID-19 pandemic

The Italian government has criticised EU's lack of solidarity with Italy.[370][371][372] *Politico* reported on 7 March that "EU countries have so far refused Italy's plea for help fighting coronavirus, as national capitals worry that they may need to stockpile face masks and other medical gear to help their own citizens, officials and diplomats said."[373] Maurizio Massari, Italy's ambassador to the EU, said that "Only China responded bilaterally. Certainly, this is not a good sign of European solidarity."[374] Serbian President Aleksandar Vučić said that "European solidarity does not exist. That was a fairy tale."[374]



In retrospective, only a few countries developed testing strategies timely

Though the theory behind testing is sensible, testing strategies widely differed across countries in the early stages of COVID-19, and numerous countries did not prioritise building a solid testing strategy.

Some of these countries argued that individuals who potentially contracted COVID-19 would not benefit from knowing whether they actually had the virus. They suggested that these individuals should stay at home in any case, isolate themselves and wait until they got better, often except for individuals with high risk of contracting COVID-19 or severely ill individuals. Furthermore, even if a country aimed to make COVID-19 tests widely available, shortages in tests, costs and a lack of skilled medical staff decreased feasibility of this approach.

Below we will illustrate how exactly testing strategies amongst countries differed, drawing on numerous interactive visuals on testing provided by the Our World in Data initiative.

Exit strategies in Europe

Most of Europe implemented strict lockdown measures to control disease spread, which have been shown to be effective at reducing transmission

As rates of new cases decline, countries are now implementing various exit strategies to relax restrictions:

Population returns to the workplace

Internal border controls were lifted in a coordinated manner

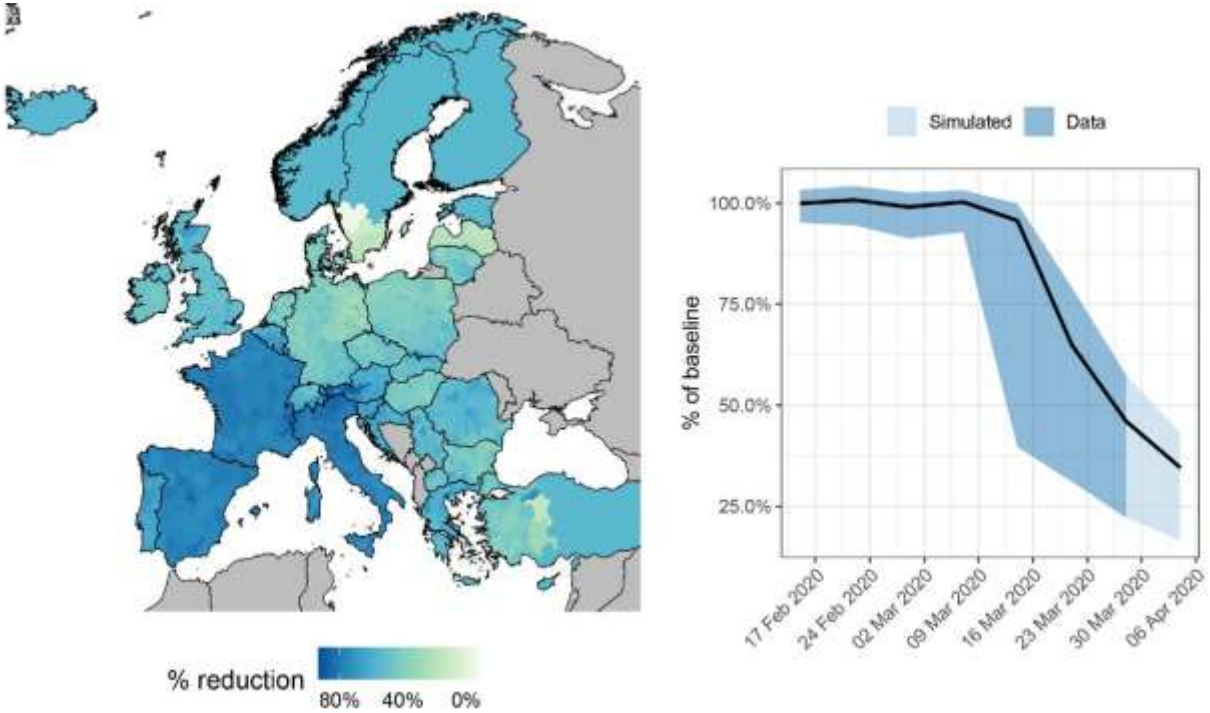
Gatherings of people are progressively permitted, and general measures are gradually be replaced by targeted ones in order to protect vulnerable groups as well as facilitate economic activity.

The Commission also develops a recovery plan, based on a new proposal for the upcoming long-term EU budget (Multiannual Financial Framework)

Actions are continuously monitored, and Member States are ready to return to stricter containment measures as necessary (United Nations Regional Information Centre, 2020)

People are advised to observe all COVID 19 prevention rules

Fig. 2 Reduction in mobility observed in NUTS3 areas from 11 Feb to 6 Apr 2020.



N. W. Ruktanonchai et al. Science 2020;science.abc5096

Science
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Thanks for your attention