Editors, authors, publishing house and translators have received no support from third parties to realize this manual.
Bernd Sebastian Kamps, M.D.
www.Amedeo.com

Christian Hoffmann, M.D.
Infektionsmedizinisches Centrum
Hamburg MVZ PartG (ICH)
ICH Stadtmitte
Glockengiesserwall 1
20095 Hamburg
researchgate.net/profile/Christian_Hoffmann8

Disclaimer
COVID medicine is a new and fast-changing field. The editors and authors of CovidReference.com have made every effort to provide information that is accurate and complete as of the date of publication. However, in view of the rapid changes occurring in medical science, COVID prevention and policy, as well as the possibility of human error, this text may contain technical inaccuracies, typographical or other errors. Readers are advised to check the trials databases (fda.gov, etc) as well as the product information currently provided by the manufacturer of each drug to be administered to verify the recommended dose, the method and duration of administration, and contraindications. It is the responsibility of the treating physician (and last-year students!) who relies on experience and knowledge about the patient to determine the best treatment and dosages for the patient. The information contained herein is provided “as is” and without warranty of any kind. The contributors to this site, including Steinhäuser Verlag, disclaim responsibility for any errors or omissions or for results obtained from the use of information contained herein.

Important: The current book is designed for educational purposes only and is not engaged in rendering medical and current historical advice or professional services. It is not a substitute for professional care. Members of the lay public using this site are advised to consult with a physician regarding personal medical care. If you have or suspect you may have a health problem, consult your healthcare provider.

This work is protected by copyright both as a whole and in part.

© 2020 by Steinhäuser Verlag
ISBN: 978-3-942687-46-1
CR 2020.5.01– Uploaded on 22 October 2020
PREFACE

Second waves, third waves, never ending waves – as the world is about to enter the second year of the SARS-CoV-2 pandemic, people realize that they are just at the beginning of a global health and economic crisis. In the Northern Hemisphere, the 6 dark autumn and winter months have begun and the world is holding its breath: will the new coronavirus follow the track of the 1918 flu epidemic, relatively mild in spring and devastating in autumn and winter?

There is no doubt that the immense resources of medicine and biotechnology will soon produce a safe and effective vaccine; however, only fools expect mass vaccinations before the middle of 2021 and a measurable impact on the pandemic before 2022.

In the meantime, people around the globe will reduce their contacts with other people and perfect their skills of social distancing. They will continue to wear face masks next year, the year after and maybe beyond. It isn’t fun but it must be done.

Bernd Sebastian Kamps & Christian Hoffmann
22 October 2020
PREFACE TO THE FIRST EDITION

Seventeen years ago, in the middle of the outbreak, we decided to write a short medical text about the ongoing SARS drama, presenting the scientific data and providing real-time updates. After publishing three editions in 6 months, a scientific magazine concluded that our SARS Reference (www.SARSReference.com) was “not fancy”, but presented “plenty of information”. When we became aware of the new coronavirus epidemic in mid-January 2020, we immediately felt that time had come to repeat our millennium exercise.

While SARS-CoV-2 seems under control in China, the epidemic is moving west briskly. What only weeks ago seemed an impossible feat – imposing and enforcing strict quarantine measures and isolating millions of people – is now a reality in many countries. People all over the world will have to adapt and invent new lifestyles in what is the most disruptive event since World War II.

We believe that the current situation needs a new type of textbook. Humanity is confronting an unknown and threatening disease which is often severe and fatal. Health care systems are overwhelmed. There is no proven treatment and vaccines will not be available soon. Such a situation has not existed since the flu pandemic in 1918.

We believe a clear head is crucial in times of over-information, with dozens of scientific papers published every day, news about hundreds of studies being planned or already on the way and social media blending hard data with rumors and fake news. The tedious work of screening the scientific literature and the scientific data has to be done – regularly & constantly, like a Swiss watch.

Over the coming months, COVID Reference will be presenting updates on a weekly basis and narrating the scientific data as coherently as possible.

Remember Science Magazine. It isn’t fancy.

Bernd Sebastian Kamps & Christian Hoffmann

29th March 2020
CONTRIBUTING AUTHORS

Thomas Kamradt, M.D.
Professor of Immunology
President, German Society of Immunology
Institute of Immunology
University Hospital Jena
Leutragraben 3
D – 07743 Jena
linkedin.com/in/thomas-kamradt-93816ba5

Stefano Lazzari, M.D.
Specialist in Public Health and Preventive Medicine
International Consultant in Global Health
Former WHO Director
linkedin.com/in/stefano-lazzari-79a933a

Jennifer Neubert, M.D.
Department of Pediatric Oncology,
Hematology and Clinical Immunology
Center for Child and Adolescent Health
Medical Faculty
Heinrich-Heine-University Düsseldorf

Tim Niehues, M.D.
Centre for Child and Adolescent Health
Helios Klinikum Krefeld
Lutherplatz 40
D – 47805 Krefeld
https://www.researchgate.net/profile/Tim_Niehues
COVID REFERENCE INTERNATIONAL

All collaborators are volunteers

Español

Anisha Gualani Gualani
Medical student, Universidad de Sevilla-US

Jesús García-Rosales Delgado
Medical student, Universidad de Sevilla-US

Italiano

Alberto Desogus
Emeritus oncologist, Oncological Hospital, Cagliari

Stefano Lazzari
M.D., Specialist in Public Health and Preventive Medicine
International Consultant in Global Health
Former WHO Director

Grazia Kiesner (Italian)
Medical Student, Università degli Studi di Firenze

Português

Joana Catarina Ferreira Da Silva
Medical student, University of Lisbon

Sara Mateus Mahomed
Medical student, University of Lisbon

Français

Bruno Giroux
M. D., Paris

Georges Mion
Professor, M.D., Service d’anesthésie réanimation, Hôpital Cochin Paris
Türkçe

Zekeriya Temircan
Ph.D. in Health/Clinic Psychology
Neuropsychology Department
Turkey

Füsun Ferda Erdoğan
Professor, Erciyes University Neurology Department/
Pediatric Neurology
Gevher Nesibe Genom and Stem Cell Institute Neuroscience Department
Turkey

Dilara Güngör
İstanbul University/Çapa Medical School Student
Turkey

Türev Demirtas
M.D., Erciyes University Faculty of Medicine
History of Medicine and Ethics Department
Kayseri / Turkey.

Tiếng Việt

Khanh Phan Nguyen Quoc
M.D., Oxford University Clinical Research Unit

Nam Ha Xuan
Medical student, Hue University of Medicine and Pharmacy

Kim Le Thi Anh (Vietnamese)
Medical student, School of Medicine and Pharmacy, Vietnam National University
Hanoi

Deutsch

Ulf Lüdeke
www.Sardinienintim.com
Copy-Editor

Rob Camp

Art

Attilio Baghino
Cover

Félix Prudhomme
YouTube: IYENSS

Thomas Splettstösser
SciStyle (Figures)
CONTENT

0. Top 10 13

1. Epidemiology 15

2. Transmission 16
   Introduction 16
   The Virus 17
   Person-to-person transmission 19
   Routes of Transmission 20
   Transmission Event 28
   Outlook 39
   New References (5th Edition) 40
   References (all) 57

3. Prevention 74
   Introduction 74
   Containment or mitigation of COVID-19? 91
   Conclusion 92
   References 92

4. Virology 110

5. Immunology 111

6. Diagnostic Tests and Procedures 112

7. Clinical Presentation 113

8. Treatment 114
9. Severe COVID 115
10. Comorbidities 116
11. Pediatrics 117
12. The First Seven Months 118
0. Top 10

1. Epidemiology

Bernd Sebastian Kamps
Stefano Lazzari
2. Transmission

Bernd Sebastian Kamps
Christian Hoffmann

Figure 1. Transmission of a SARS-CoV-2. 1) After coughing, sneezing, shouting and even after speaking – particularly loud speaking –, large droplets (green) drop to the ground around the young man. 2) In addition, some droplets, small and lightweight enough (red), are transported by air currents over longer distances (WHO 20200709). The second – aerosol – transmission is now recognized as a possibly relevant transmission route in the SARS-CoV-2. Adapted from Morawska 2020. Art work: Félix Prudhomme – IYENSS.

Introduction

Viruses have substantially influenced human health, interactions with the ecosphere, and societal history and structures (Chappell 2019). In a highly connected world, microbial evolution is boosted and pathogens exploit human behaviors to their own benefit (Morens 2013). This was critically shown during the SARS epidemic in 2003 (Kamps-Hoffmann 2003), the outbreak of Middle East Respiratory Syndrome coronavirus (MERS-CoV) (Zaki 2012), the last great Ebola epidemic in West Africa (Arwady 2015, Heymann 2015) and the Zika epidemic in 2015-2017 (Fauci 2016). Over the same time period, more virulent strains of known respiratory pathogens – H5N1 influenza virus, tuberculosis, avian H7N9 influenza virus – have emerged (Kamps-Hoffmann 2006, Jassal 2009, Gao 2013).
The Virus

SARS-CoV-2, Severe Acute Respiratory Syndrome coronavirus 2, is a highly transmissible ‘complex killer’ (Cyranoski 2020) that forced half of humanity, 4 billion people, to bunker down in their homes in the early spring of 2020. The respiratory disease rapidly evolved into a pandemic (Google 2020). In most cases, the illness is asymptomatic or paucisymptomatic and self-limited. A subset of infected individuals has severe symptoms and sometimes prolonged courses (Garner 2020). Around 10% of infected people need hospitalization and around one third of them treatment in intensive care units. The overall mortality rate of SARS-CoV-2 infection seems to be less than 1%.

Coronaviruses are tiny spheres of about 70 to 80 nanometers (a millionth of a millimeter) on thin-section electron microscopy (Perlman 2019). Compared to the size of a human, SARS-CoV-2 is as small as a big chicken compared to the planet Earth (El País). The raison d’être of SARS-CoV-2 is to proliferate, like that of other species, for example H. sapiens sapiens who has been successful in populating almost every corner of the world, sometimes at the expense of other species. SARS-CoV-2, for now, seems to be on a similarly successful track. By 7 June, only a handful of countries can claim to have been spared by the pandemic.

SARS-CoV-2’s global success has multiple reasons. The new coronavirus hijacks the human respiratory system to pass from one individual to another when people sneeze, cough, shout and speak. It is at ease both in cold and in warm climates; and, most importantly and unlike the two other deadly coronaviruses SARS-CoV and MERS-CoV, it manages to get transmitted to the next individual before it develops symptoms in the first one (see below, Asymptomatic Infection, page 30). There is no doubt that SARS-CoV-2 has a bright future – at least until the scientific community develops a safe vaccine (see the chapter Immunology, page xxx) and efficient drugs.

SARS-CoV-2 and its kin

SARS-CoV-2 is a coronavirus like

- SARS-CoV (cousin from the 2002/2003 epidemic),
- MERS-CoV (Middle East Respiratory Syndrome coronavirus),
- and a group of so-called CAR coronoviruses (for Community-Acquired Respiratory CoVs: 229E, OC43, NL63, HKU1).

The CAR group of viruses are highly transmissible and produce about 15 to 30% of common colds, typically in the winter months. On the contrary, SARS-CoV and MERS-CoV have case fatality rates of 10% and 34%, respectively, but
they never achieved pandemic spread. SARS-CoV-2, from a strictly viral point of view, is the shooting star in the coronavirus family: it combines high transmissibility with high morbidity and mortality.

SARS-CoV-2 is a virus like other commonly known viruses that cause human disease such as hepatitis C, hepatitis B, Ebola, influenza and human immunodeficiency viruses. (Note that the differences between them are bigger than those between humans and amebas.) With the exception of influenza, these viruses have a harder time infecting humans than SARS-CoV-2. Hepatitis C virus (HCV), a major cause of chronic and often fatal liver disease, is mainly transmitted by percutaneous exposure to blood, by unsafe medical practices and, less frequently, sexually. The human immunodeficiency virus (HIV), in addition to exposure to blood and perinatal transmission, also exploits sexual contact as a potent transmission route. Hepatitis B virus (HBV) is an even more versatile spreader than HCV and HIV as it can be found in high titers in blood, cervical secretions, semen, saliva, and tears; even tiny amounts of blood or contaminated secretions can transmit the virus. Ideal infection environments for HBV include, for example, schools, institutions and hospitals where individuals are in close and prolonged contact.

Of note, apart from HIV and hepatitis B and C, most viral diseases have no treatment. For example, there is no treatment for measles, polio, or smallpox. For influenza, decades of research have produced two specific drugs which have not been able to demonstrate reduced mortality – despite tests on thousands of patients. After 35 years of research, there is still no vaccine to prevent HIV infection.

Ecology of SARS-CoV-2

SARS-CoV-2 is present at high concentrations in the upper and lower respiratory tract (Zhu N 2020, Wang 2020, Huang 2020). The virus has also been found, albeit at low levels, in the kidney, liver, heart, brain, and blood (Puelles 2020). Outside the human body, the virus is more stable at low temperature and low humidity conditions, whereas warmer temperatures and higher humidity shorten the half-life (Matson 2020). It has also been shown to be detectable as an aerosol (in the air) for up to three hours, up to 24 hours on cardboard and up to two to three days on plastic and stainless steel (van Doremalen 2020). As expected, viral RNA was more likely to be found in areas immediately occupied by COVID-19 patients than in other hospital areas (Zhou J 2020). Another study documented contamination of toilets (toilet bowl, sink, and door handle) and air outlet fans (Ong SWX 2020). This is in line with the experience from MERS where many environmental surfaces of
patients’ rooms, including points frequently touched by patients or healthcare workers, were contaminated by MERS-CoV (Bin 2016).

Person-to-person transmission

Person-to-person transmission of SARS-CoV-2 was established within weeks of identification of the first cases (Chan JF 2020, Rothe 2020). Shortly after, it was suggested that asymptomatic individuals would probably account for a substantial proportion of all SARS-CoV-2 transmissions (Nishiura 2020, Li 2020). Viral load can be high 2-3 days before the onset of symptoms and almost half of all secondary infections are supposed to be caused by presymptomatic patients (He 2020).

A key factor in the transmissibility of SARS-CoV-2 is the high level of viral shedding in the upper respiratory tract (Wolfel 2020), even among paucisymptomatic patients. Pharyngeal virus shedding is very high during the first week of symptoms, with a peak at > 7 x 10^8 RNA copies per throat swab on day 4. Infectious virus was readily isolated from samples derived from the throat or lung. That distinguishes it from SARS-CoV, where replication occurred mainly in the lower respiratory tract (Gandhi 2020); SARS-CoV and MERS-CoV infect intrapulmonary epithelial cells more than cells of the upper airways (Cheng PK 2004, Hui 2018). The shedding of viral RNA from sputum appears to outlast the end of symptoms and seroconversion is not always followed by a rapid decline in viral load (Wolfel 2020). This contrasts with influenza where persons with asymptomatic disease generally have lower quantitative viral loads in secretions from the upper respiratory tract than from the lower respiratory tract and a shorter duration of viral shedding than persons with symptoms (Ip 2017).

A recently published review summarized the evidence of human SARS-CoV-2 transmission (Meyerowitz 2020). Their key points:

1. Respiratory transmission is the dominant mode of transmission.
2. Vertical transmission occurs rarely; transplacental transmission has been documented.
3. Direct contact and fomite transmission are presumed but are likely only an unusual mode of transmission.
4. Although live virus has been isolated from saliva and stool and viral RNA has been isolated from semen and blood donations, there are no reported cases of SARS-CoV-2 transmission via fecal-oral, sexual, or bloodborne routes. To date, there is 1 cluster of possible fecal-respiratory transmission.
5. Cats and ferrets can be infected and transmit to each other, but there are no reported cases to date of transmission to humans; minks transmit to each other and to humans.

Routes of Transmission
SARS-CoV-2 is spread predominantly via virus-containing droplets through sneezing, coughing, or when people interact with each other for some time in close proximity (usually less than one metre) (ECDC 2020, Chan JF 2020, Li Q 2020, Liu Y 2020). These droplets can then be inhaled or land on surfaces where they can be detectable for up to four hours on copper, up to 24 hours on cardboard and up to two to three days on plastic and stainless steel (van Doremalen 2020, Aboubakr 2020). Other people may come into contact with these droplets and get infected when they touch their nose, mouth or eyes (Wang Y 2020, Deng W 2020). SARS-CoV-2 environmental contamination around COVID-19 patients is extensive, and hospital IPC procedures should account for the risk of fomite, and potentially airborne, transmission of the virus (Santarpia 2020).

Respiratory transmission
SARS-CoV-2 is transmitted via (macro-)droplets greater than 5-10 μm in diameter, commonly referred to as respiratory droplets, and via smaller particles, < 5μm in diameter, which are referred to as droplet nuclei or aerosols. The almost century-old dichotomy (Wells 1934) “droplets vs. aerosol transmission” has been challenged by SARS-CoV-2. It is now accepted that there is no real evidence that SARS-CoV-2 pathogens should be carried only in large droplets (Fennelly 2020). At the beginning of the current pandemic, aerosol transmission of SARS-CoV-2 was generally not accepted; however, over the months, it became evident that some COVID-19 clusters, for example in choirs (Hamner 2020, Miller 2020), shopping malls (Cai J 2020), restaurants (Li Y 2020 + Lu J 2020), meat processing plants (Günter 2020, The Guardian) or vertically aligned flats connected by drainage pipes in the master bathrooms (Kang M 2020, Gormley 2020), were best explained by aerosol transmission.

On July 9 2020, WHO updated its information about SARS-CoV-2 transmission (WHO 20200709), “There have been reported outbreaks of COVID-19 in some closed settings, such as restaurants, nightclubs, places of worship or places of work where people may be shouting, talking, or singing. In these outbreaks, aerosol transmission, particularly in these indoor locations where there are crowded and inadequately ventilated spaces where infected persons spend long periods of time with others, cannot be ruled out.” In the preceding days,
a group of more than 200 scientists led by Lidia Morawska and Donald K. Milton had published a three-page warning: *It is Time to Address Airborne Transmission of COVID-19* (see also LM’s first alert on 10 April and the overviews by Prather, Wang and Schooley as well as Jayaweera 2020 et al.). As always, discordant views have been voiced, arguing that long-range aerosol-based transmission is not the dominant mode of SARS-CoV-2 transmission (Klompas 2020) and that the main mode of transmission of SARS-CoV-2 is short range through droplets and close contact (Chagla 2020). Today, aerosol transmission of SARS-CoV-2 is an accepted notion.

Viruses are released during exhalation, talking, and coughing in micro-droplets small enough to remain aloft in the air and pose a risk of exposure at distances beyond 1 to 2 m from an infected individual (Morawska 2020b). Morawska, Milton et al. suggested the following measures to mitigate airborne transmission of SARS-CoV-2:

- Provide sufficient and effective ventilation (supply clean outdoor air, minimize recirculating air) particularly in public buildings, workplace environments, schools, hospitals, and retirement care homes.
- Supplement general ventilation with airborne infection controls such as local exhaust, high efficiency air filtration, and germicidal ultraviolet lights.
- Avoid overcrowding, particularly in public transport and public buildings.

A precautionary approach to COVID-19 prevention is shown in Table 1.

The evidence for aerosol transmission and resulting recommendations for prevention have been sublimely summarized by Prather et al. in five sentences: “Respiratory infections occur through the transmission of virus-containing droplets (>5 to 10 μm) and aerosols (<5 μm) exhaled from infected individuals during breathing, speaking, coughing, and sneezing. Traditional respiratory disease control measures are designed to reduce transmission by droplets produced in the sneezes and coughs of infected individuals. However, a large proportion of the spread of coronavirus disease 2019 (COVID-19) appears to be occurring through airborne transmission of aerosols produced by asymptomatic individuals during breathing and speaking (Morawska 2020, Anderson 2020, Asadi 2019). Aerosols can accumulate, remain infectious in indoor air for hours, and be easily inhaled deep into the lungs. For society to resume, measures designed to reduce aerosol transmission must be implemented, including universal masking and regular, widespread testing to identify and isolate infected asymptomatic individuals (Prather 2020).”
Table 1. Reducing the transmission of SARS-CoV-2

<table>
<thead>
<tr>
<th>Transmission route</th>
<th>Prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. (Macro-)Droplets (&gt; 5 µm)</td>
<td>Face masks + social distancing</td>
</tr>
<tr>
<td>2. Aerosol (micro-droplets, ≤ 5µm)</td>
<td>• Face masks • Improved ventilation (open doors and windows; upgrade ventilation systems) • Improved air filtering • Avoidance of crowded and closed spaces</td>
</tr>
<tr>
<td>3. Fomites</td>
<td>Handwashing</td>
</tr>
</tbody>
</table>

For mechanical systems, organizations such as ASHRAE (the American Society of Heating, Ventilating, and Air Conditioning Engineers) and REHVA (the Federation of European Heating, Ventilation and Air Conditioning Associations) have provided guidelines based on the existing evidence of airborne transmission (Morawska 2020b).

A recent demonstration of aerosol production visualizes speech-generated oral fluid droplets and underlines that even normal speaking may be an important mode of transmission (Bax 2020). The authors provide videos showing speech droplets emitted by four people, when speaking the phrase “spit happens” with the face positioned about 10–15 cm behind a thin sheet of intense green laser light (video: https://www.youtube.com/watch?v=ooVjNth4ut8). Previously, experimental support for aerosol transmission of SARS-CoV-2 came from studies that visualized droplet formation at the exit of the mouth during violent expiratory events such as sneezing and coughing (Scharfman 2016, Bourouiba 2020; see also the video). These studies showed that the lifetime of a droplet could be considerably longer than previously assumed. When analyzed with highly sensitive laser light scattering, loud speech was found to be able to emit thousands of oral fluid droplets per second which could linger in the air for minutes (Anfinrud 2020, Stadnytskyi 2020; see also the movies showing the experimental setup and the critical comment by Abbas 2020). Loud and persistent shouting as would be usual in noisy, closed and stagnant air environments (meat packing facilities, discos, pubs, etc.) is now believed to produce the same number of droplets as produced by coughing (Chao 2020). Speech and other vocal activities such as singing have also been shown to generate air particles, with the rate of emission corresponding to voice loudness (Asadi 2019).

Of note, during the 2003 SARS epidemic, an airborne route of transmission also appeared to be a plausible explanation for the so-called Amoy Garden outbreak. On that occasion, the virus was aerosolized within the confines of very small bathrooms and may have been inhaled, ingested or...
transmitted indirectly by contact with fomites as the aerosol settled (WHO 2003).

Recognizing that SARS-CoV-2 is transmitted via aerosol has even more far-reaching consequences – personal, professional, societal and economic – in situations of community COVID-19 outbreaks. At the personal level (reminder: 20% of infected individuals are thought to transmit 80% of SARS-CoV-2 cases, so minimizing the probability of coming close to such super-spreader individuals is imperative), people might wish to avoid prolonged meetings with people from outside their inner-core “friends-and-family-bubble”; inside the bubble, meetings should be restricted to a handful of people. For everyday life, the following five *rules of thumb* are helpful:

1. Wear face masks in public spaces.
2. Keep a distance of 2 (two!) meters to other people.
3. Avoid *crowded* places (more than 5-10 people).
4. Avoid in particular *crowded* and *closed* spaces (even worse: air-conditioned closed places where air is being moved around).
5. Avoid in any circumstances *crowded*, *closed* and *noisy* spaces where people must shout to communicate. These are SARS-CoV-2’s preferred playgrounds.

At the professional level, healthcare workers will require nothing short of optimal protection. As N95 respirators achieve better filtration of airborne particles than medical masks, they should be recommended for all inpatient care of patients with COVID-19, not only during aerosol generating procedures (Dau 2020). Guideline recommendations that do not support N95 use for all inpatient COVID-19 management should consider reevaluating the existing data.

At the societal level, the attendance of important biographic events such as weddings, baptisms, circumcisions and funerals may need to be limited to a handful of intimate friends and family (probably less than 10). Religious services and recreational activities such as team sport and choir singing may not be possible.

At the economic level, all activities which bring numerous people from outside the “friends-and-family-bubbles” together may be banned during new community outbreaks. Instead of complete lockdowns like those enacted during the spring of 2020 – and which are not economically sustainable – partial lockdowns would target places where strangers or simply unacquainted people meet: discos, amusement parks, bars, restaurants, brothels and many more. Other activities such as meat processing plants might need major re-
structuring before resuming work. Re-opening schools in September has been and remains a world-wide challenge.

If SARS-CoV-2 is transmitted airborne for several meters, previous prevention recommendations of frequent hand-washing and maintaining a distance of at least one meter (arm’s length) (WHO 20200329) are insufficient. Instead, adequate control measures would include wearing suitable masks whenever infected persons may be nearby and providing adequate ventilation of enclosed spaces where such persons are known to be or may recently have been (Morawska 2020, Somsen 2020, Meselson 2020). Infrastructure may have to be adjusted, for example, Heating, Ventilation and Air Conditioning Systems (HVAC) in buildings and on ships (Correia 2020, Gormley 2020). Most of all, tighter prevention recommendations will have unforeseeable consequences for all places where foreigners, strangers or simply unacquainted people meet. SARS-CoV-2 will thus continue to impact cultural and economic life – theaters, cinemas, bars, restaurants, shops, etc – for some time to come.

In the meantime, the discussion about SARS-CoV-2 and aerosols continues. Even the droplet/aerosol terminology has now been questioned by advocates of a new distinction between aerosols and droplets using a size threshold of 100 μm, not the historical 5 μm (Prather 2020). The authors argue that this size more effectively separates their aerodynamic behavior, ability to be inhaled, and efficacy of interventions. Viruses in droplets (larger than 100 μm) typically fall to the ground in seconds within 2 m of the source and can be sprayed like tiny cannonballs onto nearby individuals. Recently, a fourth transmission route has been hypothesized: aerosolized fomites. In this case, virus would remain viable in the environment, on materials like paper tissues and on the bodies of living animals, long enough to be aerosolized on non-respiratory dust particles that can transmit infection through the air to new mammalian hosts (Asadi 2020). In retrospective, we will one day understand that transmission of viruses is not the only conceptual framework upset by the SARS-CoV-2 virus.

**Fomites**

It is still unclear to which extent transmission via fomites (e.g., elevator buttons, hand rails, restroom taps) is epidemiologically relevant (Cai J 2020). [A fomite is any inanimate object that, when contaminated with or exposed to infectious agents such as a virus, can transfer a disease to another person.] SARS-CoV-2 seems omnipresent in the spaces inhabited by infected individuals. A protein-rich medium like airway secretions could protect the virus when it is expelled and may enhance its persistence and transmission by contaminated fomites (Pastorino 2020). For example, SARS-CoV-2 RNA was de-
ected from 58 out of 601 samples (10%) from case cabins 1-17 days after the cabins were vacated, but not from non-case cabins (Yamagishi 2020). There was no difference in the detection proportion between cabins for symptomatic (15%, 28/189) and asymptomatic cases (21%, 28/131). However, no SARS-CoV-2 virus was isolated from any of the samples. Potential drivers of the SARS-CoV-2 surface adsorption and stability in various environmental conditions have been recently discussed (Joonaki 2020).

Recently, the role of fomites in SARS-CoV-2 transmission has been questioned. Some authors find that the chance transmission through inanimate surfaces might be less frequent than hitherto assumed (Mondelli 2020) and less likely to occur in real-life conditions, provided that standard cleaning procedures and precautions are enforced. Transmission through fomites would occur only in instances where an infected person coughs or sneezes on the surface, and someone else touches that surface soon after the cough or sneeze (within 1–2 h) (Goldman 2020). In any case, even face coverings may protect indirectly against fomite transmission. After analyzing mask-wearing and face-touching behavior in public areas, one group found that mask wearing was associated with reduced face-touching behavior, especially touching of the eyes, nose, and mouth (Chen Y 2020). They conclude that the reduction of face-touching behaviors by mask wearing could contribute to curbing the COVID-19 pandemic.

**Mother-to-child**

Mother-to-child transmission doesn’t seem to be a prominent route of SARS-CoV-2 transmission. There is one report of a newborn with elevated SARS-CoV-2 IgM antibodies who was exposed for 23 days from the time of the mother’s diagnosis of COVID-19 to delivery (Dong L 2020). However, there was no evidence for intrauterine vertical transmission among another group of nine women with COVID-19 pneumonia in late pregnancy (Chen H 2020).

Vaginal (n=24) versus elective cesarean (n=16) was addressed in a study from Northern Italy. In one case a newborn had a positive test after a vaginal operative delivery (Ferrazzi 2020). Two women with COVID-19 breastfed without a mask because infection was diagnosed in the post-partum period; their newborns tested positive for SARS-CoV-2 infection. The authors conclude that although post-partum infection cannot be excluded with 100% certainty, vaginal delivery seems to be associated with a low risk of intrapartum SARS-CoV-2 transmission. There is also a case report of transplacental transmission where a 23-year-old COVID-19 patient who gave birth by cesarean section to a baby found to have the infection (Vivanti 2020). The viral load was much higher in the placental tissue than in the amniotic fluid or maternal blood:
this suggests the presence of the virus in placental cells, which is consistent with findings of inflammation seen at histological examination (the baby was fine).

SARS-CoV-2 has been found in breast milk (Wu Y 2020, Groß 2020, Bastug 2020). In one study, SARS-CoV-2 RNA was detected in one milk sample, but the viral culture for that sample was negative. These data suggest that SARS-CoV-2 RNA does not represent replication-competent virus and that breast milk may not be a source of infection for the infant (Chambers 2020). As of May 2020, the Italian Society on Neonatology (SIN), endorsed by the Union of European Neonatal & Perinatal Societies (UENPS), recommended breastfeeding as advisable if a mother previously identified as COVID-19-positive or under investigation for COVID-19 was asymptomatic or paucisymptomatic at delivery. On the contrary, when a mother with COVID-19 is too sick to care for the newborn, the neonate should be managed separately and fed freshly expressed breast milk (Davanzo 2020, Davanzo 2020b [Italian]). This guidance may be subject to change in the coming months.

Stool, urine

Although no cases of fecal-oral transmission of SARS-CoV-2 have been reported thus far, a study from Zhuhai reports prolonged presence of SARS-CoV-2 viral RNA in fecal samples. Of the 41 (55%) of 74 patients with fecal samples that were positive for SARS-CoV-2 RNA, respiratory samples remained positive for SARS-CoV-2 RNA for a mean of 17 days and fecal samples remained positive for a mean of 28 days after first symptom onset (Wu Y 2020). In another study, 22/133 patients, SARS-CoV-2 was still detected in the sputum or feces (up to 39 and 13 days, respectively) after pharyngeal swabs became negative (Chen 2020). In still another study, seven out of ten children contained SARS-CoV-2 virus RNA in their fecal specimens, despite all patients showing negative results in respiratory tract specimens and the median time from onset to having negative results in respiratory tract and fecal specimens was 9 days and 34.43 days, respectively (Du W 2020).

Until proof of the contrary, the possibility of fecal-oral transmission should not be excluded. Strict precautions must be observed when handling the stools of patients infected with coronavirus. Sewage from hospitals should also be properly disinfected (Yeo 2020). Fortunately, antiseptics and disinfectants such as ethanol or bleach have good activity on human coronaviruses (Geller 2012). During the SARS-CoV outbreak in 2003, where SARS-CoV was shown to survive in sewage for 14 days at 4°C and for 2 days at 20°C (Wang XW 2005), environmental conditions could have facilitated this route of transmission.
Blood products

SARS-CoV-2 is rarely detected in blood (Wang W 2020, Wolfel 2020). After screening of 2430 donations in real-time (1656 platelet and 774 whole blood), authors from Wuhan found plasma samples positive for viral RNA from 4 asymptomatic donors (Chang 2020). It remains unclear whether detectable RNA signifies infectivity.

In a Korean study, seven asymptomatic blood donors were later identified as COVID-19 cases. None of 9 recipients of platelets or red blood cell transfusions tested positive for SARS-CoV-2 RNA (Kwon 2020). More data are needed before transmission through transfusion can be declared safe.

Sexual transmission

It is unknown whether purely sexual transmission is possible. Scrupulously eluding infection via fomites and respiratory droplets during sexual intercourse would suppose remarkable acrobatics many people might not be willing to perform. Reassuringly, SARS-CoV-2 doesn’t seem to be present in semen (Guo L 2020).

Cats and dogs et al.

SARS-CoV-2 can be transmitted to cats and dogs (Newman 2020, Garigliany 2020). When inoculated with SARS-CoV-2, cats can transmit the virus to other cats (Halfmann 2020) and although none of the cats showed symptoms, all shedded virus for 4 to 5 days and developed antibody titers by day 24. In another report, two out of fifteen dogs from households with confirmed human cases of COVID-19 in Hong Kong were found to be infected. The genetic sequences of viruses from the two dogs were identical to the virus detected in the respective human cases (Sit 2020). In still another paper, 817 companion animals in northern Italy at the height of the spring 2020 epidemic were tested for SARS-CoV-2. Although no animals tested PCR positive, 3.4% of dogs and 3.9% of cats had measurable SARS-CoV-2 neutralizing antibody titers, with dogs from COVID-19 positive households being significantly more likely to test positive than those from COVID-19 negative households (Patterson 2020).

Evidence of infection of animals with SARS-CoV-2 has been shown experimentally both in vivo and in vitro for monkeys, cats, ferrets, rabbits, foxes, and hamsters (Edwards 2020). While computational models also predicted infectivity of pigs and wild boar (Santini 2020), a recent study suggested that pigs and chickens could not be infected intranasally or oculo-oronasally by SARS-CoV-2 (Schlottau 2020).
At present, it seems unlikely that animals are potential intermediate hosts in the chain of human–pet–human transmission. Only special circumstances, such as the high animal population densities encountered on infected mink farms, might put humans at risk of animal-to-human transmission. In any case, persons with COVID-19 should be advised to avoid contact with animals. Companion animals that test positive for SARS-CoV-2 should be monitored and separated from persons and other animals until they recover (Newman 2020).

Transmission Event
Transmission of a virus from one person to another depends on four variables:
1. The nature of the virus;
2. The nature of the transmitter;
3. The nature of the transmitee (the person who will become infected);
4. The transmission setting.

Virus
In order to stay in the evolutionary game, all viruses have to overcome a series of challenges. They must attach to cells; fuse with their membranes; release their nucleic acid into the cell; manage to make copies of themselves; and have the copies exit the cell to infect other cells. In addition, respiratory viruses must make their host cough and sneeze to get back into the environment again. Ideally, this happens before the hosts realize that they are sick. This is all the more amazing as SARS-CoV-2 is more like a piece of computer code than a living creature in sensu strictu (its 30,000 DNA base pairs are a mere 100,000th of the human genetic code). That doesn't prevent the virus from being ferociously successful:

- It attaches to the human angiotensin converting enzyme 2 (ACE2) receptor (Zhou 2020) which is present not only in nasopharyngeal and oropharyngeal mucosa, but also in lung cells, such as in type II pneumocytes. SARS-CoV-2 thus combines the high transmission rates of the common coronavirus NL63 (infection of the upper respiratory tract) with the severity of SARS in 2003 (lower respiratory tract);
- It has a relatively long incubation time of around 5 days (influenza: 1-2 days), thus giving it more time to spread;
- It is transmitted by asymptomatic individuals.
As mentioned above, SARS-CoV-2 can be viable for days (van Doremalen 2020). Environmental factors that might influence survival of the virus outside the human body will be discussed below (page 38).

The virologic determinants of more or less successful SARS-CoV-2 transmission are not yet fully understood.

**Transmittor**

The mean incubation of SARS-CoV-2 infection is around 5 days (Lauer 2020, Li 2020, Zhang J 2020, Pung 2020), comparable to that of the coronaviruses causing SARS or MERS (Virlogeux 2016). Almost all symptomatic individuals will develop symptoms within 14 days of infection (Bai Y 2020). Infectiousness seems to peak on or before symptom onset (He X 2020).

It is currently unknown if SARS-CoV-2 transmission correlates with the following characteristics of the index case (transmittor):

- Symptom severity;
- Large concentrations of virus in the upper and lower respiratory tract;
- SARS-CoV-2 RNA in plasma;
- In the future: reduced viral load due to drug treatment (like in people treated for HIV infection) [Cohen 2011, Cohen 2016, LeMessurier 2018]

There are some first hints that symptom severity of the index case has an impact on transmission probability. In one study of 3410 close contacts of 391 SARS-CoV-2 infected index cases, the secondary attack rate increased with the severity of index cases, from 0.3% for asymptomatic to 3.3% for mild, 5.6% for moderate, and 6.2% for severe or critical cases (Luo L 2020). Index cases with expectoration were associated with higher risk for secondary infection (13.6% vs. 3.0% for index cases without expectoration).

SARS-CoV-2 transmission certainly correlates with a still ill-defined “super-spreader status” of the infected individual. For unknown reasons, some individuals are remarkably contagious, capable of infecting dozens or hundreds of people, possibly because they breathe out many more particles than others when they talk (Asadi 2019), shout, cough or sneeze. Transmission of SARS-CoV and MERS-CoV as well occurred to a large extent by means of super-spreading events (Peiris 2004, Hui 2018). Super-spreading has been recognized for years to be a normal feature of disease spread (Lloyd-Smith 2005). One group suggested that 80% of secondary transmissions could be caused by around 20% of infectious individuals (Adam 2020). A value called the dispersion factor (k) describes this phenomenon. The lower the k is, the more transmission comes from a small number of people (Kupferschmidt 2020,
Tufekci 2020; if you like the FT, read also *To beat Covid-19, find today’s super-spreading ‘Typhoid Marys’*). While SARS was estimated to have a $k$ of 0.16 (Lloyd-Smith 2005) and MERS of 0.25, in the flu pandemic of 1918, in contrast, the value was about one, indicating that clusters played less of a role (Endo 2020). For the SARS-CoV-2 pandemic, the dispersion factor ($k$) is currently thought to be higher than for SARS and lower than for the 1918 influenza (Endo 2020, Miller 2020, On Kwok 2020, Wang L 2020).

Transmission is more likely when the infected individual has few or no symptoms because no one will take notice and maintain precautions. Around half of secondary cases are supposed to be transmitted during the pre-symptomatic stage of the index case (He X 2020). *Asymptomatic transmission* of SARS-CoV-2 – proven a few weeks after the beginning of the pandemic (Bai Y 2020) – has justly been called the Achilles’ heel of the COVID-19 pandemic (Gandhi 2020). As shown during an outbreak in a skilled nursing facility, the percentage of asymptomatic individuals can be as high as 50% early (Arons 2020; most of these individuals would later develop some symptoms). Importantly, SARS-CoV-2 viral load was comparable in individuals with typical and atypical symptoms, and in those who were pre-symptomatic or asymptomatic. Seventeen of 24 specimens (71%) from pre-symptomatic persons had viable virus by culture 1 to 6 days before the development of symptoms (Arons 2020), suggesting that SARS-CoV-2 may be shed at high concentrations before symptom development.

Note that although SARS-CoV-2 is highly transmissible, given the right circumstances and the right prevention precautions, *zero transmission* is possible. In one case report, there was no evidence of transmission to 16 close contacts, among them 10 high-risk contacts, from a patient with mild illness and positive tests for up to 18 days after diagnosis (Scott 2020).

To what extent children contribute to the spread of SARS-CoV-2 infection in a community is unknown. Infants and young children are normally at high risk for respiratory tract infections. The immaturity of the infant immune system may alter the outcome of viral infection and is thought to contribute to the severe episodes of influenza or respiratory syncytial virus infection in this age group (Tregoning 2010). Until now, however, there is a surprising absence of pediatric patients with COVID-19, something that has perplexed clinicians, epidemiologists, and scientists (Kelvin 2020).

Although a retrospective study among individuals hospitalized in Milan showed that only about 1% of children and 9% of adults without any symptoms or signs of SARS-CoV-2 infection tested positive for SARS-CoV-2 (Milani 2020) – suggesting a minor role of children in transmission –, children can be the source for important outbreaks. Twelve children who acquired SARS-CoV-
2 infection in child-care facilities – all with mild or no symptoms – transmitted the virus to at least 12 (26%) of 46 non-facility contacts (Lopez 2020). Family gatherings are well-known settings for widespread SARS-CoV-2 transmission. In an outbreak that occurred during a 3-week family gathering of five households, an adolescent aged 13 years was the suspected primary patient. Among the 14 persons who stayed in the same house, 12 experienced symptoms (Schwartz 2020). Of note, none of the additional six family members who maintained outdoor physical distance without face masks during two longer visits (10 and 3 hours) to the family gathering developed symptoms.

Although the discovery of a pediatric inflammatory multisystem syndrome (PIMS) in SARS-CoV-2 infection in children (Verdoni 2020, Viner 2020, ECDC 15 May 2020) came as a surprise, the fact that children are susceptible to SARS-CoV-2 infection but frequently do not have notable disease raises the possibility that children could be an important source of viral transmission and amplification in the community. There is an urgent need for further investigation of the role children have in SARS-CoV-2 transmission chains (Kelvin 2020).

Health authorities should know that SARS-CoV-2 infected individuals do not need to be quarantined for weeks. Persistently positive RT-PCRs generally do not reflect replication-competent virus. SARS-CoV-2 infectivity rapidly decreases to near-zero after about 10 days in mild-to-moderately-ill patients and 15 days in severely-to-critically-ill and immunocompromised patients (Rhee 2020). Of note, RT-PCR cycle threshold (Ct) values (a measure for viral load) correlated strongly with cultivable virus. In one study, the probability of culturing virus declined to 8% in samples with Ct > 35 and to 6% (95% CI: 0.9–31.2%) 10 days after onset; it was similar in asymptomatic and symptomatic persons (Singanayagam 2020).

In any potential transmission setting, face coverings reduce the transmission of SARS-CoV-2. Among 139 clients exposed to two symptomatic hair stylists with confirmed COVID-19 while both the stylists and the clients wore face masks, not a single symptomatic secondary case was observed; among 67 clients tested for SARS-CoV-2, all tests were negative (Hendrix 2020). At least one hair stylist was infectious: all four close household contacts (presumably without masks) became ill. Unfortunately, face masks don’t work everywhere – and not for everyone. In some countries, infected individuals claimed the right to not wear face coverings in the name of liberty (they forgot that an individual’s liberty ends where it infringes on the liberties of others). Interestingly, social distancing compliance can be predicted by individual differences in working memory (WM) capacity. WM retains a limited amount of information over a short period of time at the service of other ongoing men-
tal activities. Limited WM capacity constrains mental functions while extended capacities are often associated with better cognitive and affective outcomes. The hidden message in the paper by Weizhen Xie et al: if the guy sitting next to you in the bus does not wear a mask, don’t insist. His working memory capacity is poor (Xie W 2020). Change seats.

**Transmittee**

Upon exposure to SARS-CoV-2, the virus may come in contact with cells of the upper or lower respiratory tract of an individual. After inhalation, larger respiratory droplets are filtered by the nose or deposited in the oropharynx, whereas smaller droplet nuclei are carried by the airstream into the lungs where their site of deposition depends on their mass, size and shape and is governed by various mechanisms (Dhand 2020).

Numerous cell entry mechanisms of SARS-CoV-2 have been identified that potentially contribute to the immune evasion, cell infectivity, and wide spread of SARS-CoV-2 (Shang J 2020). (The pathogenesis of COVID-19 will be discussed in an upcoming separate COVID Reference chapter.) Susceptibility to SARS-CoV-2 infection is probably influenced by the host genotype (Williams 2020). This would explain the higher percentage of severe COVID-19 in men (Piccininni 2020) and possibly the similar disease course in some twins in the UK (The Guardian, 5 May 2020).

A high percentage of SARS-CoV-2 seronegative individuals have SARS-CoV-2 reactive T cells. This is explained by previous exposure to other coronaviruses (“common cold” coronaviruses) which have proteins that are highly similar to those of SARS-CoV-2. It is still unclear whether these cross-reactive T cells confer some degree of protection, are inconsequential or even potentially harmful if someone who possesses these cells becomes infected with SARS-CoV-2 (Braun 2020, Grifoni 2020).

The “right” genotype may not be sufficient in the presence of massive exposure, for example by numerous infected people and on multiple occasions as might happen, for example, in health care institutions being overwhelmed during the beginning of an epidemic. It is known from other infectious diseases that viral load can influence the incidence and severity of disease. Although the evidence is limited, high infection rates among health workers have been attributed to more frequent contact with infected patients, and frequent exposure to excretia with high viral load (Little 2020).

Recently, it has been shown that rigorous social distancing not only slowed the spread of SARS-CoV-2 in a cohort of young, healthy adults but also prevented symptomatic COVID-19 while still inducing an immune response.
After an outbreak in two Swiss army companies (company 2 and 3, see Table 2), 62% of tested soldiers were found to have been exposed to SARS-CoV-2 and almost 30% had COVID-19 symptoms. In company 1 where strict distancing and hygiene measures (SDHMs) had been implemented after the outbreak in companies 2 and 3, only 15% had exposure to SARS-CoV-2, but none of them had COVID-19 symptoms. (The Swiss army SDHMs: keep a distance of at least 2 m from each other at all times; wear a surgical face mask in situations where this cannot be avoided [e.g., military training]; enforce a distance of 2 m between beds and during meals; clear and disinfect all sanitary facilities twice daily; separate symptomatic soldiers immediately.)

Table 2: Baseline characteristics of the study population on March 31, 2020

<table>
<thead>
<tr>
<th></th>
<th>Company 1</th>
<th>Company 2</th>
<th>Company 3</th>
<th>Company 2+3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soldiers</td>
<td>154</td>
<td>200</td>
<td>154</td>
<td>354</td>
</tr>
<tr>
<td>Tested*</td>
<td>88</td>
<td>130</td>
<td>51</td>
<td>181</td>
</tr>
<tr>
<td>Exposed to SARS-CoV-2**</td>
<td>13/88 (15%)</td>
<td>83/130 (64%)</td>
<td>30/51 (59%)</td>
<td>113/181 (62%)</td>
</tr>
<tr>
<td>COVID-19***</td>
<td>0 (0%)</td>
<td>54/200 (27%)</td>
<td>48/154 (31%)</td>
<td>102/354 (29%)</td>
</tr>
</tbody>
</table>

* More than 50% of the soldiers of all companies were sampled on April 14.
** On April 14, detection of SARS-CoV-2 in nasopharyngeal swabs or by positive serology test for immunoglobulin A, G or M.

The authors cautiously suggested that quantitatively reducing the viral inoculum received by SARS-CoV-2 virgin recipients not only reduced the probability of infection but also could have caused asymptomatic infections in others while still being able to induce an immunological response (Bielecki 2020), and idea that was later echoed by Monica Gandhi and George W. Rutherford (Ghandi 2020).

If genes offer no protection, behavior may do so. In the coming autumn and winter months 2020/2021, face covering is paramount. It reduces, for example, the number of infections among hospital personnel. In March 2020, the Mass General Brigham, the largest health care system in Massachusetts (12 hospitals, > 75,000 employees), implemented universal masking of all HCWs and patients with surgical masks. During the pre-intervention period, the SARS-CoV-2 positivity rate increased exponentially, with a case doubling time of 3.6 days. During the intervention period, the positivity rate decreased linearly from 14.65% to 11.46% (Wang X 2020). In Paris, in a 1500-bed adult and a 600-bed pediatric setting of a university hospital, the total number of HCW
cases peaked on March 23rd, then decreased slowly, concomitantly with a continuous increase in preventive measures (including universal medical masking and PPE) (Contejean 2020). In Chennai, India, before the introduction of face shields, 12/62 workers were infected while visiting 5880 homes with 31,164 persons (222 positive for SARS-CoV-2). After the introduction of shields among 50 workers (previously uninfected) who continued to provide counseling, visiting 18,228 homes with 118,428 persons (2682 positive), no infection occurred (Bhaskar 2020). The preventive measures are not new to medicine – surgeons have been using personal protective equipment (PPE) for more than a century (Stewart 2020). The wearing of masks by adults also remains critical to reducing transmission in child-care settings (Link-Gelles 2020).

Masks work even with super-emitters. By measuring outward emissions of micron-scale aerosol particles by healthy humans performing various expiratory activities, William D. Ristenpart, Sima Asadi and colleagues found that both surgical masks and unvented KN95 respirators reduced the outward particle emission rates by 90% and 74% on average during speaking and coughing. These masks similarly decreased the outward particle emission of a coughing super-emitter, who for unclear reasons emitted up to two orders of magnitude more expiratory particles via coughing than average (Asadi 2020). An interesting collateral finding is that people speak more loudly, but do not cough more loudly, when wearing a mask.

After visualizing the flow fields of coughs under various mouth covering scenarios, a recently published study (Simha 2020) found that

1. **N95 masks are the most effective at reducing the horizontal spread of a cough (spread: 0.1 and 0.25 meters).**
2. **A simple disposable mask can reduce the spread to 0.5 meters, while an uncovered cough can travel up to 3 meters.**
3. **Coughing into the elbow is not very effective. Unless covered by a sleeve, a bare arm cannot form the proper seal against the nose necessary to obstruct airflow and a cough is able to leak through any openings and propagate in many directions.**

Although the data regarding the effectiveness of face masks is now clear, will everyone understand, i.e., even individuals with a still functioning working memory? If some individuals continue to put themselves at risk of SARS-CoV-2 infection (as well as their friends and relatives in case of infection), what are the drivers of behaviors that might influence risk for COVID-19 exposure among young adults? In a remote US county, the drivers were low severity of disease outcome; peer pressure; and exposure to misinformation, conflicting
messages, or opposing views regarding masks (Wilson 2020). A scientifically inspired national prevention policy will be needed to counter misinformation and – let’s speak frankly for just two seconds! – address human stupidity. First, public health officials need to ensure that the public understands clearly when and how to wear cloth face coverings properly. Second, innovation is needed to extend physical comfort and ease of use. Third, the public needs consistent, clear, and appealing messaging that normalizes community masking (Brooks 2020). The authors get the point: a small adaption in our daily lives relies on a highly effective low-tech solution that can help turn the tide.

Transmission setting

The transmission setting, i.e., the actual place where the transmission of SARS-CoV-2 occurs, is the final element in the succession of events that leads to the infection of an individual. High population density which facilitates super-spreading events (see also chapter Epidemiology, Transmission Hotspots, page Fehler! Textmarke nicht definiert.) is key to widespread transmission of SARS-CoV-2.

In the early phase of the pandemic, hospitals and other health care centers have sometimes been hotspots of SARS-CoV-2 transmission, either because of ignorance or missing protective equipment. In a major London teaching hospital, 66/435 (15%) of COVID-19 inpatient cases between 2 March and 12 April 2020 were definitely or probably hospital-acquired through varied transmission routes (case fatality: 36%) (Rickman 2020).

In a prospective international multicentre cohort study of 1718 healthcare workers participating in 5148 at-risk tracheal intubation episodes, the overall incidence of the primary endpoint (lab-confirmed COVID-19 diagnosis or new symptoms requiring self-isolation or hospitalisation) was 10.7% over a median of 32 days (El-Boghdadly 2020).

In Greece, healthcare personnel represented approximately 10% of all notified COVID-19 cases. Those with high-risk occupational exposure to COVID-19 had increased probability of serious morbidity, healthcare seeking, hospitalization and absenteeism (Maltezou 2020).

In the University of Washington medical system and its affiliated organizations, between March 12 and April 23, a total of 3477 symptomatic employees were tested; 185 (5.3%) employees tested positive for COVID-19. The prevalence of SARS-CoV-2 was similar when comparing frontline HCWs (5.2%) to non-frontline staff (5.5%) (Mani 2020).
Awaiting results from (difficult) randomised trials, the currently best available evidence suggests for all public and healthcare settings (Chu DK 2020) the FPE protection triad of

- Physical distancing of at least 1 m, even better 2 m.
- Face mask, ideally N95 or similar.
- Eye protection (mandatory in healthcare settings and similar).

Find a helpful video, demonstrating the complex procedure for putting on and removing PPE as recommended by the CDC (Ortega 2020). It is safe and cheap to assume that SARS-CoV-2 is everywhere (Lednicky 2020).

**Indoor environments**

Indoor environments are SARS-CoV-2’s preferred playgrounds. In one modeling study, the authors estimated that viral load concentrations in a room with an individual who was coughing frequently were very high, with a maximum of 7.44 million copies/m³ from an individual who was a high emitter (Riediker 2020). However, regular breathing from an individual who was a high emitter was modeled to result in lower room concentrations of up to 1248 copies/m³. They conclude that the estimated infectious risk posed by a person with typical viral load who breathes normally was low and that only a few people with very high viral load posed an infection risk in the poorly ventilated closed environment simulated in this study.

Clusters of cases have been reported in many, predominantly indoor, settings. Viable virus from air samples was isolated from samples collected 2 to 4.8 meters away from two COVID-19 patients (Lednicky 2020). The genome sequence of the SARS-CoV-2 strain isolated was identical to that isolated from the NP swab from the patient with an active infection. Estimates of viable viral concentrations ranged from 6 to 74 TCID50 units/L of air. During the first months of the pandemic, most clusters were found to involve fewer than 100 cases, with the exceptions being in healthcare (hospitals and elderly care), large religious gatherings and large co-habitation settings (worker dormitories and ships). Other settings with examples of clusters between 50–100 cases in size were schools, sports, bars, shopping centers and a conference (Leclerc 2020).

Transportation in closed spaces – by bus, train or aircraft – has been shown to transmit SARS-CoV-2 at various degrees, depending on face mask use and time of travel. One paper describes a bus ride in a vehicle 11.3 meters long and 2.5 meters wide with 49 seats, fully occupied with all windows closed and the ventilation system on during the 2.5-hour trip. Among the 49 passengers
(including the driver) who shared the ride with the index person, eight tested positive and eight developed symptoms. The index person sat in the second-to-last row, and the infected passengers were distributed over the middle and rear rows (Luo K 2020). An even more informative paper describes 68 individuals (including the source patient) taking a bus on a 100-minute round trip to attend a worship event. In total, 24 individuals (35%) received a diagnosis of COVID-19 after the event. The authors were able to identify seats for each passenger and divided bus seats into high-risk and low-risk zones (Shen Y 2020). Passengers in the high-risk zones had moderately but non-significantly higher risk of getting COVID-19 than those in the low-risk zones. On the 3-seat side of the bus, except for the passenger sitting next to the index patient, none of the passengers sitting in seats close to the bus window developed infection. In addition, the driver and passengers sitting close to the bus door also did not develop infection, and only 1 passenger sitting by an operable window developed infection. The absence of a significantly increased risk in the part of the bus closer to the index case suggested that airborne spread of the virus may at least partially explain the markedly high attack rate observed. Lesson learned for the future? If you take the bus, choose seats near a window – and open it!

To answer the question how risky train traveling is in the COVID-19 era, one group analyzed passengers in Chinese high-speed trains. They quantified the transmission risk using data from 2334 index patients and 72,093 close contacts who had co-travel times of 0–8 hours from 19 December 2019 through 6 March 2020. Unsurprisingly, travelers adjacent to an index patient had the highest attack rate (3.5%) and the attack rate decreased with increasing distance but increased with increasing co-travel time. The overall attack rate of passengers with close contact with index patients was 0.32% (Hu M 2020).

A recently published review about in-flight transmission of SARS-CoV-2 finds that the absence of large numbers of confirmed and published in-flight transmissions of SARS-CoV is encouraging but not definitive evidence that fliers are safe (Freedman 2020). At present, based on circumstantial data, strict use of masks appears to be protective. In previous studies, SARS-CoV-2 transmission has been described onboard aircrafts (Chen J 2020, Hoehl 2020). Note that if you don’t wear a mask, business class will not protect you from infection. A Vietnamese group report on a cluster among passengers on VN54 (Vietnam Airlines), a 10-hour commercial flight from London to Hanoi on March 2, 2020 (at that time, the use of face masks was not mandatory on airplanes or at airports) (Khanh 2020). Affected persons were passengers, crew, and their close contacts. The authors traced 217 passengers and crew to their final destinations and interviewed, tested, and quarantined them. Among the
16 persons in whom SARS-CoV-2 infection was detected, 12 (75%) were passengers seated in business class along with the only symptomatic person (attack rate 62%). Seating proximity was strongly associated with increased infection risk (risk ratio 7.3, 95% CI 1.2–46.2).

Transmission clusters, partly linked to super-spreader events, have been reported since the very beginning of the SARS-CoV-2 pandemic:

- Business meeting, Southern Germany, 20-21 January (Rothe 2020)
- Cruise Ship, Yokohama, Japan, 4 February (Rocklov 2020)
- Church meeting, Daegu, Korea, 9 and 16 February (Kim 2020)
- Religious gathering, Mulhouse, France, 17-24 February (Kuteifan 2020)
- Medical advisory board meeting, Munich, Germany, 20-21 (Hijnen 2020)
- Nursing facility, King County, Washington, 28 February (McMichael 2020)
- Aircraft carriers: Theodore Roosevelt (Payne 2020) + Charles-de-Gaulle, March (Le Monde)
- Choir (Hamner 2020)
- Concert (Plautz 2020)
- Homeless shelter, Boston, 28 March (Baggett 2020)

A study of 1407 transmission pairs that formed 643 transmission clusters in mainland China identified 34 super-spreaders, with 29 super-spreading events occurring outside households (Xu XK 2020).

**Temperature and climate**

Another variable still poorly understood is ambient temperature and humidity.

**SARS-CoV-1 (2003):** The transmission of coronaviruses can be affected by several factors, including the climate (Hemmes 1962). Looking back to the 2003 SARS epidemic, we find that the stability of the first SARS virus, SARS-CoV, depended on temperature and relative humidity. A study from Hong Kong, Guangzhou, Beijing, and Taiyuan suggested that the SARS outbreak in 2002/2003 was significantly associated with environmental temperature. The study provided some evidence that there was a higher possibility for SARS to reoccur in spring than in autumn and winter (Tan 2005). It was shown that SARS-CoV remained viable for more than 5 days at temperatures of 22–25°C and relative humidity of 40–50%, that is, typical air-conditioned environments (Chan KH 2011). However, viability decreased after 24 h at 38°C and 80–90% relative humidity. The better stability of SARS coronavirus in an envi-
environment of low temperature and low humidity could have facilitated its transmission in subtropical areas (such as Hong Kong) during the spring and in air-conditioned environments. It might also explain why some Asian countries in the tropics (such as Malaysia, Indonesia or Thailand) with high temperature and high relative humidity environment did not have major community SARS outbreaks (Chan KH 2011).

SARS-CoV-2 (2020): It is as yet unclear as to whether and to what extent climatic factors influence virus survival outside the human body and might influence local epidemics. SARS-CoV-2 is not readily inactivated at room temperature and by drying like other viruses, for example herpes simplex virus. One study mentioned above showed that SARS-CoV-2 can be detectable as an aerosol (in the air) for up to three hours, up to four hours on copper, up to 24 hours on cardboard and up to two to three days on plastic and stainless steel (van Doremalen 2020).

A few studies suggest that low temperature might enhance the transmissibility of SARS-CoV-2 (Triplett 2020; Wang 2020b, Tobias 2020) and that the arrival of summer in the northern hemisphere could reduce the transmission of the COVID-19. A possible association of the incidence of COVID-19 and both reduced solar irradiance and increased population density has been discussed (Guasp 2020). It was reported that simulated sunlight rapidly inactivated SARS-CoV-2 suspended in either simulated saliva or culture media and dried on stainless steel plates while no significant decay was observed in darkness over 60 minutes (Ratnesar-Shumate 2020). However, another study concluded that transmission was likely to remain high even at warmer temperatures (Sehra 2020). In particular the current epidemics in Brazil and India and the southern US – areas with high temperatures – should temper hopes that COVID “simply disappears like a miracle”. Warm and humid summer conditions alone might be unlikely to limit substantially new important outbreaks (Luo 2020, Baker 2020, Collins 2020).

Outlook
Almost a year after the first SARS-CoV-2 outbreak in China, the transmission dynamics driving the pandemic are coming into focus. It now appears that a high percentage (as high as 80%?) of secondary transmissions could be caused by a small fraction of infectious individuals (10 to 20%; Adam 2020); if this is the case, then the more people are grouped together, the higher the probability that a superspreader is part of the group.

It is now acknowledged that aerosol transmission plays an important role in SARS-CoV-2 transmission (Morawska 2020b, WHO 20200709, Prather 2020); if
this is the case, then building a wall around this same group of people and putting a ceiling above them further enhances the probability of SARS-CoV-2 infection.

It finally appears that shouting and speaking loudly emits thousands of oral fluid droplets per second which could linger in the air for minutes (Anfinrud 2020, Stadnytskyi 2020, Chao 2020, Asadi 2019, Bax 2020); if this is the case, then creating noise (machines, music) around people grouped in a closed environment would create the perfect setting for a superspreader event.

Over the coming months, the scientific community will try and

- define more precisely the role of fomites in the transmission of SARS-CoV-2;
- unravel the secrets of super-spreading;
- advance our understanding of host factors involved in the successful “seeding” of SARS-CoV-2 infection;
- elucidate the role of children in the transmission of the virus at the community level;
- explicate the role of young adults in the genesis of the second European SARS-CoV-2 wave;
- continue to describe the conditions under which people should be allowed to gather in larger groups;

Without a coronavirus vaccine, nobody will return to a “normal” pre-2020 way of life. The most promising exit strategy for the coronavirus crisis is an efficient vaccine that can be rolled out safely and affordably to billions of people. Thousands of researchers are working around the clock, motivated by fame (becoming the next Dr. Salk?) and money (becoming the next Scrooge McDuck?). Until the worldwide availability of a vaccine, the only feasible prevention scheme is a potpourri of physical distancing (Kissler 2020), intensive testing, case isolation, contact tracing, quarantine (Ferretti 2020) and, as a last (but not impossible) resort, local lockdowns and curfews.

New References (5th Edition)

The Virus
In a cross-sectional observational study in a London hospital, SARS-CoV-2 was detected on 114/218 (52.3%) of surfaces and 14/31 (38.7%) air samples but no virus was cultured. As expected, viral RNA was more likely to be found in areas immediately occupied by COVID-19 patients than in other areas (Zhou J 2020).


When intranasally inoculated with TCID50 of a SARS-CoV-2 isolate, twelve fruit bats (Rousettus aegyptiacus) showed characteristics of a reservoir host and 12 ferrets (Mustela putorius) mimicked subclinical human infection with efficient spread. Pigs (Sus scrofa domesticus) and 20 chickens (Gallus gallus domesticus could not be infected by SARS-CoV-2 (Schlottau 2020).

Routes of Transmission


Eric Meyerowitz et al. present a comprehensive review of the evidence of human SARS-CoV-2 transmission (Meyerowitz 2020). Their key points:

1. Respiratory transmission is the dominant mode of transmission.
2. Vertical transmission occurs rarely; transplacental transmission has been documented.
3. Cats and ferrets can be infected and transmit to each other, but there are no reported cases to date of transmission to humans; minks transmit to each other and to humans.
4. Direct contact and fomite transmission are presumed but are likely only an unusual mode of transmission.
5. Although live virus has been isolated from saliva and stool and viral RNA has been isolated from semen and blood donations, there are no reported cases of SARS-CoV-2 transmission via fecal–oral, sexual, or bloodborne routes. To date, there is 1 cluster of possible fecal–respiratory transmission.

AEROSOL, DROPLETS


According to Kimberly Prather and colleagues, we should clarify the terminology to distinguish between aerosols and droplets using a size threshold of 100 μm, not the historical 5 μm (Prather 2020). This size more effectively separates their aerodynamic behavior, ability to be inhaled, and efficacy of interventions. Viruses in droplets (larger than 100 μm) typically fall to the ground in seconds within 2 m of the source and can be sprayed like tiny cannonballs onto nearby individuals.

Spit happens. This group published the impressive NEJM video, visualizing speech-generated oral fluid droplets and suggesting that normal speaking might be an important mode of transmission (Bax 2020). Here, the four authors vigorously resist the criticism of other authors who argued that the video experiments were unrealistic. They also provide nice new videos showing speech droplets emitted by four people, when speaking the phrase “spit happens” with the face positioned about 10–15 cm behind a thin sheet of intense green laser light.


New video: https://www.youtube.com/watch?v=ooVjNth4ut8


Is there really evidence that some pathogens are carried only in large droplets? (Fennelly 2020) Or would cough aerosols and exhaled breath from patients with various respiratory infections show striking similarities in aerosol size distributions? In case of doubt, how would you protect your family and yourself?


After evacuation from the Diamond Princess cruise ship in March 2020, 11 were admitted to a hospital in Nebraska, two in a biocontainment unit and 9 in a quarantine unit. Key features of both units included: (1) individual rooms with private bathrooms; (2) negative-pressure rooms (> 12 ACH) and negative-pressure hallways; (3) key-card access control; (4) unit-specific infection prevention and control (IPC) protocols including hand hygiene and changing of gloves between rooms; and (5) personal protective equipment (PPE) for staff that included contact and aerosol protection. Joshua Santarpia and colleagues collected air and surface samples to examine viral shedding from isolated individuals and detected viral contamination among all samples. Their data suggest that SARS-CoV-2 environmental contamination around COVID-19 patients is extensive, and hospital IPC procedures should account for the risk of fomite, and potentially airborne, transmission of the virus (Santarpia 2020).


Kamps – Hoffmann
Brief review. It is impossible to conclude that aerosol-based transmission never occurs, write Michael Klompas and colleagues, but the balance of currently available evidence suggests that long-range aerosol-based transmission is not the dominant mode of SARS-CoV-2 transmission (Klompas 2020).


Zain Chagla and colleagues discuss the paper by Morawska L, Milton DK, It is Time to Address Airborne Transmission of COVID-19 (Clin Infect Dis 2020, 6 July). They agree that there is potential for the transmission by aerosols, especially in poorly ventilated indoor crowded environments. However, they argue that the main mode of transmission of SARS-CoV-2 is short range through droplets and close contact. Explore this one-page comment to see how the debate continues (Chagla 2020).


SARS-CoV-2 can be transmitted via droplets, fomites and possibly aerosol. Will we need to get accustomed to a fourth transmission route, aerosolized fomites? That’s what Nicole Bouvier and colleagues suggest, although for now only for influenza A virus. They show that dried influenza virus remains viable in the environment, on materials like paper tissues and on the bodies of living animals, long enough to be aerosolized on non-respiratory dust particles that can transmit infection through the air to new mammalian hosts (Asadi 2020). Will we soon see a paper about SARS-CoV-2 transmission via aerosolized fomites?


Nanshan Zhong, Min Kang and colleagues report 9 infected patients in 3 families. While the first family had a history of travel to the coronavirus disease 2019 (COVID-19) epicenter Wuhan, the other 2 families had no travel history and a later onset of symptoms. The families lived in 3 vertically aligned flats connected by drainage pipes in the master bathrooms. The authors suggest that virus-containing fecal aerosols may have been produced in the associated vertical stack during toilet flushing after use by the index patients (Kang M 2020). This report reminds us of a SARS-1 outbreak in March 2003 among residents of Amoy Gardens, Hong Kong, with a total of 320 SARS cases in less than three weeks (see www.SARSReference.com, page 65).

concludes that that wastewater plumbing systems, particularly those in high-rise buildings, deserve closer investigation, both immediately in the context of SARS-CoV-2 and in the long term, because they may be a reservoir for other harmful pathogens.

**FOMITES**


Some arguments that environmental contamination leading to SARS-CoV-2 transmission is unlikely to occur in real-life conditions, provided that standard cleaning procedures and precautions are enforced. The chance of transmission through inanimate surfaces is likely less frequent than hitherto recognized (Mondelli 2020).


In the early epidemic in Japan, many infections occurred among the passengers and crew members on board the Diamond Princess cruise ship in February, 2020. By March 1, 2020, there were approximately 700 individuals with laboratory-detected SARS-CoV-2 infection (see the previous articles by Russell et al., Yamagishi et al. and Tabata et al.). The authors performed environmental sampling on the Diamond Princess cruise ship on 22-23 February 2020 (prior to disinfection of the vessel and while some passengers and crew members remained aboard) and obtained specimens from cabins in which confirmed COVID-19 cases stayed (case cabins), cabins with no confirmed case at any point (non-case cabins), and common areas. SARS-CoV-2 RNA was detected from 58 out of 601 samples (10%) from case cabins 1-17 days after the cabins were vacated, but not from non-case cabins (Yamagishi 2020). There was no difference in the detection proportion between cabins for symptomatic (15%, 28/189) and asymptomatic cases (21%, 28/131). No SARS-CoV-2 virus was isolated from any of the samples. The authors conclude that transmission risk of SARS-CoV-2 from symptomatic and asymptomatic patients may be similar and environmental surfaces could be involved in viral transmission.


Is wearing face masks really associated with reduced face-touching behaviors? To answer the question, Xing Li and colleagues from Sun Yat-sen University, Guangzhou, China, used videos recorded in public transportation stations, streets, and parks among the general population in China, Japan, South Korea, Western Europe (ie, Eng-
land, France, Germany, Spain, and Italy), and the US to analyze mask-wearing and face-touching behavior in public areas. The authors found that mask wearing was associated with reduced face-touching behavior, especially touching of the eyes, nose, and mouth (Chen Y 2020). They conclude that the reduction of face-touching behaviors by mask wearing could contribute to curbing the COVID-19 pandemic. Excellent news for the coming months.


Nice overview of existing knowledge concerning viral spread, molecular structure of SARS-CoV-2, and the stability of the virus surface. Edris Joonaki and colleagues discuss potential drivers of the SARS-CoV-2 surface adsorption and stability in various environmental conditions (Joonaki 2020).


If you are exploring extra-respiratory routes of SARS-CoV-2 transmission, read the article by Chuan Qin, Wei Deng and colleagues. The authors inoculated five rhesus macaques with SARS-CoV-2 conjunctivally, intratracheally, and intragastrically. The conjunctivally infected animal had a higher viral load in the nasolacrimal system than the intratracheally infected animal but also showed mild interstitial pneumonia, suggesting distinct viral distributions (Deng W 2020).

MOTHER-TO-CHILD


Maybe the first documented case of transplacental transmission. French doctors report on a 23-year-old COVID-19 patient who gave birth by cesarean section to a baby found to have the infection (Vivanti 2020). The viral load was much higher in the placental tissue than in the amniotic fluid or maternal blood: this suggests the presence of the virus in placental cells, which is consistent with findings of inflammation seen at histological examination. Good news: baby is fine.


There are some case reports on the detection of SARS-CoV-2 in breast milk. Christina Chambers and colleagues examined 64 breast milk samples from 18 infected women. Although SARS-CoV-2 RNA was detected in one milk sample, the viral culture for that
sample was negative. These data suggest that SARS-CoV-2 RNA does not represent replication-competent virus and that breast milk may not be a source of infection for the infant (Chambers 2020).

Cats and Dogs


Nicola Decaro and colleagues assess SARS-CoV-2 infection in 817 companion animals in northern Italy at the height of the spring 2020 epidemic. Although no animals tested PCR positive, 3.4% of dogs and 3.9% of cats had measurable SARS-CoV-2 neutralizing antibody titers, with dogs from COVID-19 positive households being significantly more likely to test positive than those from COVID-19 negative households (Patterson 2020). From their experience, the authors conclude that it is unlikely that infected pets play an active role in SARS-CoV-2 transmission to humans. Only under special circumstances, such as the high animal population densities encountered on infected mink farms, animal-to-human transmission might be likely.


Mutien Garigliany from Liège, Belgium, and colleagues report a human-to-cat transmission. A household cat was productively infected with the SARS-CoV-2 virus excreted by its owner, and the infection caused a non-fatal but nevertheless severe disease (Garigliany 2020).

Transmission Event

Transmitter


These researchers examined the added value of near real-time genome sequencing of SARS-CoV-2 in a subpopulation of infected patients during the first 10 weeks of COVID-19 containment in Australia. Genomic evidence was used to cluster 38.7% (81 out of 209) of cases for which the available epidemiological data could not identify direct links (Rockett 2020). This included clustering 12.4% (26 out of 209) of cases with a history of recent arrival from overseas with other cases without a travel history and 5.3% (11/209) of locally acquired cases with unknown epidemiological...
links. Twenty-two (10.5%) of the 209 cases were epidemiologically classified as ‘locally acquired—contact not identified’.


The authors analyzed 59,073 contacts of 5,706 COVID-19 index patients. Of 10,592 household contacts, 11.8% had COVID-19; rates were higher for contacts of children than adults. Of 48,481 non-household contacts, 1.9% had COVID-19. Interestingly, the highest COVID-19 rate (18.6%) was found for household contacts of school-aged children (Park YJ 2020) and the lowest (5.3%) for household contacts of children 0–9 years in the middle of school closure.


Early reports suggested that children, often asymptomatic, might be facilitators of SARS-CoV-2 transmission and amplify local outbreaks. Here, Carlo Agostini, Gregorio Milani and colleagues conducted a study among individuals hospitalized in Milan. About 1% of children and 9% of adults without any symptoms or signs of SARS-CoV-2 infection tested positive for SARS-CoV-2. The authors conclude that their data do not support the hypothesis that children are at higher risk of carrying SARS-CoV-2 asymptomatically than adults (Milani 2020). Attention: a retrospective analysis.


Chen Mao and colleagues traced 3410 close contacts of 391 SARS-CoV-2 infected index cases between 13 January and 6 March 2020. 127 contacts (3.7%) were secondarily infected. Compared with the household setting (10.3%), the secondary attack rate was lower for exposures in healthcare settings (1.0%) and on public transportation (0.1%). Interestingly, although not unexpectedly, the secondary attack rate increased with the severity of index cases, from 0.3% for asymptomatic to 3.3% for mild, 5.6% for moderate, and 6.2% for severe or critical cases (Luo L 2020). Index cases with expectoration were associated with higher risk for secondary infection (13.6% vs. 3.0% for index cases without expectoration).

Xie W, Campbell S, Zhang W. Working memory capacity predicts individual differences in social-distancing compliance during the COVID-19 pandemic in the

Among 850 US residents participating in a survey, the authors found that social distancing compliance could be predicted by individual differences in working memory (WM) capacity. WM retains a limited amount of information over a short period of time at the service of other ongoing mental activities. Its limited capacity constrains our mental functions, such that higher WM capacity is often associated with better cognitive and affective outcomes. Of note, the unique contribution of WM capacity to the individual differences in social distancing compliance could not be explained by other psychological and socioeconomic factors (e.g., moods, personality, education, and income levels). The message that the authors hide using scientific language can be said more clearly: if you see a guy sitting in the bus not wearing a mask: poor idiot, don’t get closer. His WM capacity is poor (Xie W 2020).


Persistently positive RT-PCRs generally do not reflect replication-competent virus. SARS-CoV-2 infectivity rapidly decreases thereafter to near-zero after about 10 days in mild-to-moderately-ill patients and 15 days in severely-to-critically-ill and immunocompromised patients (Rhee 2020). This review summarizes evidence-to-date on the duration of infectivity of SARS-CoV-2.


More on “viral load” and infectivity. Virus culture was attempted from 324 samples (from 253 cases) that tested positive for SARS-CoV-2 by RT-PCR. RT-PCR cycle threshold (Ct) values correlated strongly with cultivable virus. Probability of culturing virus declined to 8% in samples with Ct > 35 and to 6% (95% CI: 0.9–31.2%) 10 days after onset; it was similar in asymptomatic and symptomatic persons (Singanayagam 2020).


Same direction. This prospective serial sampling of 70 patients revealed clinically relevant cycle thresholds (Ct, “viral load”), namely a Ct of 24 (“high viral load”), 34, and > 40 (“negative”) that occurred 9, 26, and 36 days after symptom onset. Of note, race, gender, or corticosteroids did not appear to influence RNA-positivity. A retrospective analysis of 180 patients revealed that initial Ct did not correlate with requirement for admission or intensive care (Lesho 2020).
Cuc Tran, Adriana Lopez and colleagues describe 12 children who acquired SARS-CoV-2 infection in child-care facilities. All had mild or no symptoms. They transmitted the virus to at least 12 (26%) of 46 non-facility contacts (Lopez 2020). The authors conclude that testing children who might not have symptoms could improve control of transmission from child-care attendees to family members.


Children can serve as the source for COVID-19 outbreaks, even when their symptoms are mild (Schwartz 2020). In this outbreak that occurred during a 3-week family gathering of five households, an adolescent aged 13 years was the suspected primary patient. Among the 14 persons who stayed in the same house, 12 experienced symptoms. Of note, none of the additional six family members who maintained outdoor physical distance without face masks during two longer visits (10 and 3 hours) to the family gathering developed symptoms.

TRANSMITTER


Nathaniel M Lewis and colleagues sought to estimate the household secondary infection rate (SIR) of SARS-CoV-2 and evaluate potential risk factors for secondary infection among 58 households in Utah and Wisconsin. Fifty-two of 188 household contacts acquired secondary infections (SIR: 28%, 95% CI: 22–34%). Of note, household contacts to COVID-19 patients with immunocompromised conditions had increased odds of infection (OR: 15.9, 95% CI: 2.4–106.9) as well as household contacts who themselves had diabetes mellitus (OR: 7.1, 95% CI: 1.2–42.5) (Lewis 2020).

Still in the US: Which are the drivers of behaviors that might influence risk for COVID-19 exposure among young adults? In a remote US County, these were low severity of disease outcome; peer pressure; and exposure to misinformation, conflicting messages, or opposing views regarding masks (Wilson 2020). A scientifically inspired national prevention policy would have been helpful.


Masks work with super-emitters! William D. Ristenpart, Sima Asadi and colleagues measured outward emissions of micron-scale aerosol particles by healthy humans performing various expiratory activities while wearing different types of medical-grade or homemade masks. Both surgical masks and unvented KN95 respirators reduced the outward particle emission rates by 90% and 74% on average during speaking and coughing. These masks similarly decreased the outward particle emission of a coughing super-emitter, who for unclear reasons emitted up to two orders of magnitude more expiratory particles via coughing than average (Asadi 2020). An interesting collateral finding: people speak more loudly, but do not cough more loudly, when wearing a mask.


Have we ever mentioned masks? Among 139 clients exposed to two symptomatic hair stylists with confirmed COVID-19 while both the stylists and the clients wore face masks, not a single symptomatic secondary case was observed; among 67 clients tested for SARS-CoV-2, all tests were negative (Hendrix 2020). At least one hair stylist was infectious: all four close household contacts (presumably without masks) became ill.


Again, universal masking: in March 2020, the Mass General Brigham, the largest health care system in Massachusetts (12 hospitals, > 75,000 employees), implemented universal masking of all HCWs and patients with surgical masks. During the preintervention period, the SARS-CoV-2 positivity rate increased exponentially, with a case doubling time of 3.6 days. During the intervention period, the positivity rate decreased linearly from 14.65% to 11.46%, with a weighted mean decline of 0.49% per day and a net slope change of 1.65% additional decline per day compared with the preintervention period (Wang X 2020).

This prospective study compared a 1,500-bed adult and a 600-bed pediatric setting of a university hospital located in central Paris. From February 24th until April 10th, 2020, all symptomatic HCW were screened. Attack rates were of 3.2% and 2.3% in the adult and pediatric setting, respectively (p = 0.0022). In the adult setting, HCW more frequently reported exposure to COVID-19 patients without PPE (25% versus 15%, p = 0.046) (Contejean 2020). The total number of HCW cases peaked on March 23rd, then decreased slowly, concomitantly with a continuous increase in preventive measures (including universal medical masking and PPE). Residual transmissions were related to exposures with undiagnosed patients or colleagues but not to contacts with children attending out-of-home care facilities.


Data is clear now. First, public health officials need to ensure that the public understands clearly when and how to wear cloth face coverings properly. Second, innovation is needed to extend physical comfort and ease of use. Third, the public needs consistent, clear, and appealing messaging that normalizes community masking (Brooks 2020). According to the authors, **broad adoption of cloth face coverings is a civic duty**, a small adaption in our daily lives reliant on a highly effective low-tech solution that can help turn the tide.


Are you a surgeon? Then your particular medical association has been **using personal protective equipment (PPE) for more than a century** (Stewart 2020). This review addresses both the mechanism of SARS-CoV-2 transmission and the capabilities of PPE in the perioperative COVID-19 setting.


This observational study describes transmission before and after the use of face shields (made of polyethylene terephthalate) in health workers in Chennai, India. Before the introduction of face shields, 12/62 workers were infected, while visiting 5,880 homes with 31,164 persons (222 positive for SARS-CoV-2). After the introduction, among 50 workers (previously uninfected) who continued to provide counseling, visit-
ing 18,228 homes with 118,428 persons (2682 positive), no infection occurred (Bhaskar 2020).


Ruth Link-Gelles et al. report a possible secondary transmission in four of the 666 child-care programs in Rhode Island that were allowed to reopen. The apparent absence of secondary transmission within the other 662 child-care programs was likely the result of efforts to contain SARS-CoV-2 transmission, in particular maximum class sizes and use of face masks for adults (Link-Gelles 2020). The authors conclude that adherence to current CDC recommendations remains critical to reducing transmission in child-care settings, including wearing of masks by adults, limiting mixing between established student-teacher groups, staying home when ill, and cleaning and disinfecting frequently touched surfaces.


Fine droplets can pass through layers of masks and are carried away by the exhaled airflow unlike larger droplets that settle down due to gravity. Now Padmanabha Prasanna Simha and Prasanna Simha Mohan Rao visualize the flow fields of coughs under various mouth covering scenarios. The results:

4. N95 masks are the most effective at reducing the horizontal spread of a cough (spread: 0.1 and 0.25 meters).

5. A simple disposable mask can reduce the spread to 0.5 meters, while an uncovered cough can travel up to 3 meters.

6. Coughing into the elbow? Not very effective! Unless covered by a sleeve, a bare arm cannot form the proper seal against the nose necessary to obstruct airflow and a cough is able to leak through any openings and propagate in many directions (Simha 2020).

**TRANSMISSION SETTING**


ISCHGL, Austria — They came from across the world to ski in the most famous resorts of the Austrian alps... (Gebrekidan 2020).

John A. Lednicky and colleagues isolated viable virus from air samples collected 2 to 4.8 meters away from two COVID-19 patients (Lednicky 2020). The genome sequence of the SARS-CoV-2 strain isolated was identical to that isolated from the NP swab from the patient with an active infection. Estimates of viable viral concentrations ranged from 6 to 74 TCID50 units/L of air.


Review of outbreaks during flights. According to the authors, the absence of large numbers of confirmed and published in-flight transmissions of SARS-CoV is encouraging but not definitive evidence that fliers are safe. At present, based on circumstantial data, strict use of masks appears to be protective (Freedman 2020). Structured prospective studies to quantitate transmission risk on flight with rigid masking protocols are now most pressing.


The authors report a cluster of cases among passengers on VN54 (Vietnam Airlines), a 10-hour commercial flight from London to Hanoi on March 2, 2020. Among the 16 persons in whom SARS-CoV-2 infection was detected, 12 (75%) were passengers seated in business class along with the only symptomatic person (attack rate 62%) (Khanh 2020). The authors find that blocking middle seats, currently recommended by the airline industry, may in theory prevent some in-flight transmission events but seems to be insufficient to prevent superspreading events. They conclude that the risk for onboard transmission of SARS-CoV-2 during long flights is real and has the potential to cause COVID-19 clusters of substantial size, even in business class–like settings with spacious seating arrangements well beyond the established distance used to define close contact on airplanes. (Note that at the time, March 2, the use of face masks was not mandatory on airplanes or at airports, and there was no social distancing on the aircraft.)

Among 335 passengers on a flight from Singapore to Hangzhou in China (a Boeing 787, 5-hour flight, seat occupancy 89%), a total of 16 COVID-19 patients were diagnosed among all passengers, yielding an attack rate of 4.8%. However, after careful investigation, only one case was identified who appears to have become infected during the flight (Chen J 2020). He was seated near four infected passengers from Wuhan for approximately an hour (he had moved a seat) and did not wear his facemask correctly during the flight. The sources of infection in the other 15 passengers were complex and the passengers could have acquired their infections in Wuhan before the tour, or during the group tour before boarding.


Two likely SARS-CoV-2 transmissions on a 4.5-hour flight from Tel Aviv to Frankfurt, with 7 index cases. Both passengers were seated within two rows of an index case (Hoehl 2020). According to the authors, it could be speculated that the rate may have been reduced further had the passengers worn masks.


Is keeping 2 meters away enough to stay safe from a trumpet at full blast? Try it, find out! Introduce five student musicians – a soprano singer and clarinet, flute, French horn, and trumpet players — in a clean room one at a time and let them perform a short solo piece (Plautz 2020).


How risky is train traveling in the COVID-19 era? To answer this question, analyze passengers in Chinese high-speed trains. Jinfeng Wang and colleagues quantified the transmission risk using data from 2,334 index patients and 72,093 close contacts who had co-travel times of 0–8 hours from 19 December 2019 through 6 March 2020. Unsurprisingly, travelers adjacent to an index patient had the highest attack rate (3.5%) and the attack rate decreased with increasing distance, but increased with increasing co-travel time. The overall attack rate of passengers with close contact with index patients was 0.32% (Hu M 2020). The author’s conclusion: during COVID outbreaks, when travelling on public transportation in confined spaces such as trains, increase seat distance and reduce passenger density.

If you take the bus, choose seats near a window (and open it). On January 19, 2020, 68 individuals (including the source patient) took a bus on a 100-minute round trip to attend a worship event. In total, 24 (35%) received a diagnosis of COVID-19 after the event. The authors were able to identify seats for each passenger and divided bus seats into high-risk and low-risk zones (Shen Y 2020). Passengers in the high-risk zones had moderately but non-significantly higher risk of getting COVID-19 than those in the low-risk zones. On the 3-seat side of the bus, except for the passenger sitting next to the index patient, none of the passengers sitting in seats close to the bus window developed infection. In addition, the driver and passengers sitting close to the bus door also did not develop infection, and only 1 passenger sitting by an operable window developed infection. The absence of a significantly increased risk in the part of the bus closer to the index case suggested that airborne spread of the virus may at least partially explain the markedly high attack rate observed.


Transmission in a bus. The tour coach was 11.3 meters long and 2.5 meters wide with 49 seats, fully occupied with all windows closed and the ventilation system on during the 2.5-hour trip. Among the 49 passengers (including the driver) who shared the ride with the index person, eight tested positive and eight developed symptoms (Luo K 2020). The index person sat in the second-to-last row, and the infected passengers were distributed over the middle and rear rows.


Eating and drinking and socializing? Everything may well return to normal in about two years. In the meantime, note that adults with a positive SARS-CoV-2 test result were found to be twice as likely to have had dinner at a restaurant than those with negative test results (Fisher 2020). Kiva Fisher and colleagues conclude that eating and drinking on-site at locations that offer such options might be important risk factors associated with SARS-CoV-2 infection. Bars and restaurants are in for a rough autumn and winter season.


In this modeling study, Michael Riediker from the Swiss Centre for Occupational and Environmental Health in Winterthur and Dai-Hua Tsai from the University Hospital of
Psychiatry in Zurich, Switzerland, it is estimated that viral load concentrations in a room with an individual who was coughing frequently were very high, with a maximum of 7.44 million copies/m$^3$ from an individual who was a high emitter (Riediker 2020). However, regular breathing from an individual who was a high emitter was modeled to result in lower room concentrations of up to 1248 copies/m$^3$. They conclude that the estimated infectious risk posed by a person with typical viral load who breathes normally was low and that only a few people with very high viral load posed an infection risk in the poorly ventilated closed environment simulated in this study.

In late March 2020, a large outbreak on the aircraft carrier USS Theodore Roosevelt was characterized by widespread transmission with relatively mild symptoms and asymptomatic infection among mostly young, healthy adults with close, congregate exposures. One fifth of infected participants reported no symptoms. Preventive measures, such as using face-coverings and observing social distancing, reduced risk for infection: among 382 service members, those who reported taking preventive measures had a lower infection rate than did those who did not report taking these measures (e.g., wearing a face-covering, 56% versus 81%; avoiding common areas, 54% versus 68%; and observing social distancing, 55% versus 70%, respectively) (Payne 2020).


Dillon Adam, Peng Wu and colleagues identified 4–7 superspreading events (SSEs) across 51 clusters ($n = 309$ cases) and estimate that 19% (95% confidence interval, 15–24%) of cases seeded 80% of all local transmissions (Adam 2020). After controlling for age, transmission in social settings was associated with more secondary cases than households when controlling for age. Social settings are likely to become major battle grounds of coming SARS-CoV-2 waves.


Super-spreading events are an important phenomenon in the transmission of many diseases (such as SARS-CoV-1, MERS-CoV, Ebola virus, etc.), in which certain individuals infect a disproportionately large number of people. Here Yuhai Bi, Liang Wang and colleagues show that super-spreading events played an important role in the early stage of the COVID-19 outbreak. They estimated the dispersion parameter to be 0.23 (95% CI: 0.13–0.39) (Wang L 2020). (What is the dispersion parameter? Check this FT article: To beat Covid-19, find today’s superspreading ‘Typhoid Marys’)

Tufekci Z. This Overlooked Variable Is the Key to the Pandemic. The Atlantic 2020, published 30 September. Full-text:

Even non-scientists have heard about R0 (pronounced as “r-naught”)—the basic reproductive number of a pathogen, a measure of its contagiousness on average. But even some scientists may have not yet encountered k, the measure of its dispersion. If you haven’t done it before, do it now: explore k. It’s simply a way of asking whether a virus spreads in a steady manner or in big bursts, whereby one person infects many, all at once (Tufekci 2020).

References (all)

COVID Reference ENG 005


Chu DK, Akl EA, Duda S, et al. Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and
**meta-analysis.** The Lancet, June 1. Full-text: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31142-9/fulltext


COVID Reference ENG 005


Garner P. For 7 weeks I have been through a roller coaster of ill health, extreme emotions, and utter exhaustion. The BMJ Opinion, 5 May 2020. Full-text: https://blogs.bmj.com/bmj/2020/05/05/paul-garner-people-who-have-a-more-protracted-illness-need-help-to-understand-and-cope-with-the-constantly-shifting-bizarre-symptoms/ (accessed 16 May 2020)


Kamps – Hoffmann


Leclerc QJ et al. What settings have been linked to SARS-CoV-2 transmission clusters? Wellcome Open Res 2020, 5:83. Full-text: https://doi.org/10.12688/wellcomeopenres.15889.1

Leclerc QJ, Fuller NM, Knight LE, Funk S, CMMID COVID-19 Working Group, Knight GM. What settings have been linked to SARS-CoV-2 transmission clusters? Wellcome Open Res 2020, 5:83. Full-text: https://doi.org/10.12688/wellcomeopenres.15889.1


Miller D, Martin AM, Harel N, et al. **Full genome virus sequences inform patterns of SARS-CoV-2 spread into and within Israel.** medRxiv 22 May 2020. Full-text: https://doi.org/10.1101/2020.05.21.20104521


Santini J, Edwards SJL. Host range of SARS-CoV-2 and implications for public health. Lancet Microbe 2020; published online June 18. Full-text: https://doi.org/10.1016/S2666-5247(20)30069-0


COVID Reference ENG 005


Triplett M. Evidence that higher temperatures are associated with lower incidence of COVID-19 in pandemic state, cumulative cases reported up to March 27. medRxiv pre-print, 12 April 2020. Full-text: https://doi.org/10.1101/2020.04.02.20051524


3. Prevention
Stefano Lazzari

Introduction
In the absence of an effective vaccine or antiviral treatment, prevention through public health measures remains the mainstay of SARS-COV-2 infection control and pandemic impact mitigation. Effective preventive measures for respiratory infections have been standard practices for many years. However, uncertainties still exist about the role and importance of different transmission routes in the spread of SARS-COV-2 (See chapter on Transmission). This complicates the choices in terms of the most efficient and effective mix of public health measures to be implemented and the correct prevention messages to be communicated to the public.

The basic COVID-19 preventive strategies include: the identification and isolation of infectious cases and quarantine for suspected cases and close contacts; changes in individual behaviors including physical and social distancing, use of face masks and hand hygiene; travel restrictions, bans on mass gatherings and localized or nationwide lockdowns when the other measures prove ineffective in halting the spread of the virus. Specific prevention measures can be simple recommendations left to the decision of the individual, or mandatory measures to be implemented under control by the public health authorities. Preventive measures can therefore be applied at the personal, community and societal level.

In this chapter we will review the available scientific evidence on the effectiveness of these measures in reducing the spread of SARS-COV-2.

Prevention at the personal level

Good respiratory hygiene/cough etiquette.
Good respiratory hygiene refers to measures aimed at containing respiratory secretions and reducing their spread in the environment or to other people. (Chavis, 2019) Traditionally, they include:

- Covering your mouth and nose with a tissue or with your elbow when coughing or sneezing; and safe disposal of the tissue once used.
- Use of a surgical or tissue face mask.
- Perform hand hygiene often, and always after contact with potentially contaminated objects/materials.
Good respiratory hygiene and cough etiquette are usually recommended for individuals with signs and symptoms of a respiratory infection. However, given the established risk of SARS-COV-2 infection from asymptomatic individuals, public health authorities all over the world have recommended these measures for everybody when in public places. This is not without controversy, in particular on the use of masks in the absence of symptoms.

**Face masks**

The use of face masks to reduce the risk of infection is an established medical and nursing procedure. It is therefore surprising that it has created such a debate in the context of COVID-19. The initial recommendation by WHO and other health authorities that masks should only be used by health workers and symptomatic patients resulted in controversy among the experts and widespread confusion among the public. This was contradictory with the images of people wearing masks in all settings from countries in Asia that successfully managed to contain the pandemic. In addition, the existence of different types of masks greatly complicated communication efforts.

Face masks can prevent transmission of respiratory viruses in two ways:

1. **when worn by healthy individuals** they are protecting them from infection by reducing the exposure of the mouth and nose to viral particles present in the air or on contaminated hands;
2. **when worn by an infected person** they perform source control, by reducing the amount of virus dispersed in the environment while coughing, sneezing or talking.

Different types of masks perform these tasks differently, which also dictates the situations in which they should be used. Type of masks currently used include:

- **N95 (or FFP2) masks**, designed to block 95% of very small particles. They reduce the wearer’s exposure to particles including aerosols and large droplets. They also reduce the patient or other bystanders’ exposure to particles emitted by the wearer (unless they are equipped with a one-way valve to facilitate breathing).

- **Surgical masks** only filter effectively large particles. Being loose fitted, they will reduce only marginally the exposure of the wearer to droplets and aerosols. They do, however, limit considerably the emission of saliva or droplets by the wearer, reducing the risk of infecting other people.
• **Cloth masks** will stop droplets that are released when the wearer talks, sneezes, or coughs. As recommended by WHO, they should include multi-layers of fabric. When surgical or N95 masks are not available, cloth masks can still reduce the risk of SARS-COV-2 transmission in public places.

If masks are protective, why were they not widely recommended at the beginning of the pandemic? Whether due to poor communication, fear of shortage of essential medical supplies or under-appreciation of the role of asymptomatic carriers in spreading the virus, the initial reluctance in promoting mask use and the resulting controversy was not helpful in combating the pandemic and contributed to a general undermining of the credibility of public health authorities.

It was only on 5 June, months into the pandemic, that WHO released updated guidance on the use of masks, recognizing the role that face masks can play in reducing transmission from asymptomatic carriers in particular settings. This was a few days after the publication of a comprehensive review and meta-analysis of observational studies showing a significant reduction in risk of infection with all types of masks (Chu 2020). Surgical masks were also shown to work in a hamster model (Chan JF 2020). Other authors, based on reviews or modelling, recommend wearing suitable masks whenever an infected person may be nearby (Meselson 2020, Prather 2020, Zhang 2020). (See also the discussion on droplets and aerosol, page xxx.)

Meanwhile the controversy on the use of masks continues, including on the potential negative effects of wearing masks on health, for example on cardiopulmonary capacity (Fikenzer, 2020). Regardless of the controversy and the mounting “No-Mask” movements, face masks are “here to stay”. The sight of people wearing face masks in public, which in the past surprised and amused Western travelers to Asian countries, will be a common sight worldwide for months and maybe for years to come.

**Hand Hygiene**

The role of fomites in transmission of SARS-CoV-2 remains unclear but cannot be excluded. (Although objects can be easily contaminated by infected droplets and contaminate hands, it is extremely challenging to prove such transmission.) In any case, frequent handwashing is known to disrupt the transmission of respiratory diseases. Since people routinely make finger-to-nose or finger-to-eye contact (Kwok, 2015), handwashing of 30 seconds with ordinary soap is always recommended when there is a contact with a potentially infected item and regularly whenever possible (ex. when returning home). If water and soap are not available (ex. in public places), use of hy-
Prevention | 77

Handalcoholic solutions or gel is recommended. These solutions have been shown to efficiently inactivate the SARS-COV-2 virus in 30 seconds (Kratzel, 2020) and can be home-made using a WHO recommended formulation. Hand-hygiene has the added advantage of preventing infections from many other respiratory pathogens. Unfortunately, both water for handwashing and hydroalcoholic solutions are often not available in resource-poor settings (Schmidt, 2020)

Physical/Social distancing and avoiding crowded conditions

Physical distancing means keeping a safe distance from others. The term is often confused with the more common “social distancing”, usually imposed during lockdowns, that means reducing social contacts as much as possible by staying home and keeping away from others to prevent the spread of COVID-19.

Social distancing has been unequivocally shown to reduce the spread of SARS-CoV-2 – in Wuhan and Shanghai, daily contacts were reduced 7-8-fold during the social distancing period, with most interactions restricted to the household (Zhang J 2020b, Du Z 2020). Social distancing can be an individual choice, but it is usually imposed by health authorities during “Lockdowns” or “stay-at-home orders”. We will expand on the issues related to lockdowns and social distancing in the sections below.

With the end of lockdowns and the restart of economic and social activities, physical distancing in public places will become an important behavioural aspect of everyday life and an essential measure to reduce the spread of SARS-COV-2. Keeping a safe distance from others seems like a straightforward recommendation but defining what can be considered a “safe distance” is in fact quite complicated. In a published meta-analysis (Chu, 2020), the authors estimated that the risk of being infected with SARS-COV-2 is reduced to 13% for those standing at 1 m, further reduced to only 3% beyond that distance. Based on this evidence, the WHO and ECDC recommend a minimum inter-personal distance of 1 m, although other agencies and countries suggest 1.5 m (Australia, Italy, Germany), 1.8 m (US CDC), or even 2 meters (Canada, China, UK). (BBC News, 2020)

Some authors suggest that even 2 meters might not be sufficient and that being “safe” would depend on multiple factors related to both the individual and the environment. These could include infecting viral load, duration of exposure, number of individuals present, indoor versus outdoor settings, level of ventilation, and whether face coverings are worn or not. (Qureshi 2020, Jones 2020). In crowded conditions, including public transport (e.g. trains,
buses, metros), physical distancing is often impossible and the use of a protective mask is increasingly becoming mandatory.

![Figure 1](https://example.com/image.png)

**Figure 1.** Jones NR, et al. Two metres or one: what is the evidence for physical distancing in covid-19? BMJ. 2020 Aug 25;370:m3223. Reproduced with permission.

**Speak quietly, don’t shout (or sing)!**

Traditionally, visible droplets produced during coughing and sneezing are considered the main carriers of respiratory viruses. It has only recently emerged that normal speech also yields large quantities of particles that are too small to be visible, but are large enough to carry a variety of communicable respiratory pathogens and can remain airborne for longer periods. The rate of particle emission during normal human speech is positively correlated with the loudness (amplitude) of vocalization, ranging from approximately 1 to 50 particles per second (0.06 to 3 particles per cm³), regardless of the language spoken (English, Spanish, Mandarin, or Arabic) (Asadi 2019). However, a small fraction of individuals behaves as “speech superemitters,” consistently releasing many more particles than their peers.

These data may help explain the occurrence of some super-spreaders events (e.g. choirs, parties and festivals, slaughterhouses, sport events, religious celebrations, family gatherings, etc.) that are disproportionately responsible for outbreaks of COVID-19 (See Epidemiology section). While research will con-
continue to study super-spreaders events, people should abide to a simple rule: 
*Regardless of physical distancing, speak quietly, don't shout!*

**Household hygiene**

Several studies suggest the possibility of aerosol and fomite transmission of SARS-CoV-2, since the virus can remain viable and infectious in aerosols for hours and on surfaces up to days (Doremalen 2020, Chin 2020). Though transmission of SARS-CoV-2 from contaminated surfaces has not been clearly documented, traditional good home hygiene measures like cleaning floors and furniture, keeping good ventilation and the general disinfection of frequently used objects (e.g. door and window handles, kitchen and food preparation areas, bathroom surfaces, toilets and taps, touchscreen personal devices, computer keyboards, and work surfaces) are recommended to prevent transmission, particularly where confirmed or suspected COVID-19 cases are present (CDC 2020, WHO 20200515).

SARS-CoV-2 is sensitive to ultraviolet rays and heat. Sustained heat at 56°C for 30 minutes, 75% alcohol, chlorine-containing disinfectants, hydrogen peroxide disinfectants and chloroform can effectively inactivate the virus. Common detergents and sodium hypochlorite (bleach) can also be used effectively. To avoid poisoning, disinfectants should be used at the recommended concentrations, wearing appropriate PPE and should never be mixed. US CDC reported a substantial increase in calls to the poison centers in March 2020 associated with improper use of cleaners and disinfectants; many cases were in children <5 years old (MMWR 2020).

**Chemoprophylaxis (not there yet!)**

In the future, antiviral drugs may be used to reduce viral shedding in suspected cases and as a prophylactic treatment of contacts. As for now, unfortunately, no such drugs are available.

**Prevention at the community/societal levels**

**Widespread testing, quarantine, and intensive contact tracing**

Tedros Adhanom Ghebreyesus didn’t get everything right in the SARS-CoV-2 pandemic, but he was right when he recommended: “Test! Test! Test!” (WHO, 16 March 2020). Indeed, identification, and testing of suspected cases, isolation and care for those confirmed, and tracing, testing and quarantine of close contacts are critical activities to try to break the chain of transmission in any epidemic. They worked well, for example, in responding to the 2003 SARS outbreak and many countries in Asia successfully applied them to
COVID-19 (Li 2020, Lam 2020, Park 2020). The South Korea experience has been nicely summarized in an article in The Guardian.

However, despite the early availability of sensitive PCR tests (Sheridan 2020), many countries in Europe and elsewhere were caught by surprise. Unprepared, they struggled initially to provide sufficient testing, isolation and contact tracing capacities to keep up with the pace of spread of SARS-COV-2. In Italy, the lack of laboratory capacities led to limiting PCR tests to symptomatic patients only, missing many asymptomatic cases. Other countries, like Germany, fared better in diagnostics but implementing contact tracing proved difficult everywhere when the epidemic reached its peak, due to the large number of potential contacts of asymptomatic cases and their relatively long incubation period.

Ensuring sufficient testing capacities paired with the development of new rapid diagnostic tests (see section on Diagnosis) will be essential in facing future COVID-19 clusters or the feared “second wave” of infections. Advanced pooled testing strategies (Mallapaty, 2020) and the use of saliva samples could facilitate the task by allowing the rapid testing of large number of people, as China has done by testing all the population of Wuhan (more than 10 million people) in less than 2 weeks.

**Isolation** (separation of ill or infected persons from others) and **quarantine** (the restriction of activities or separation of persons who are not ill, but who may be exposed to an infectious agent or disease) are essential measures to reduce the spread of COVID-19. Unless a patient is hospitalized, quarantine and isolation are usually done at home or in dedicated facilities like hotels, dormitories, or group isolation facilities. (CDC 2020) Given the uncertainty about the infectivity of the suspected individual, preventive measures are similar for both isolation of confirmed cases and quarantine of contacts. Basically, you are required to stay at home or in the facility and avoid non-essential contacts with others, including household members, for a set period to avoid spreading the infection.

The long incubation and high pre-symptomatic infectivity of COVID-19 puts family members of infected individuals at particular risk (Little 2020). The infection rate found for household members varies between 11% and 32% (Bi Q 2020, Wu J 2020). These differences are probably due to different isolation measures implemented inside the family homes. Ideally, people in isolation should have access to a separate bedroom (and bathroom), personal protection equipment (PPE) and should not have contacts with people at high risk of serious COVID-19 disease.
The period of isolation and quarantine required before suspected or confirmed cases can be considered no more infectious remains controversial. Initially, the requirement for a confirmed case was to have clinically recovered and to have two negative RT-PCR results on sequential samples taken at least 24 hours apart. (WHO 2020) This second criteria proved challenging in countries with limited testing capacities and even when tests are available, some patients can continue to have positive PCR results for weeks or months after the cessation of symptoms, leading to prolonged isolation periods.

Updated WHO criteria were published in June (WHO 20200617). Based on data showing the rarity of the presence of vital virus after 9 days from symptom onset (Cevic 2020), the new recommendation is to limit the isolation period to:

- 10 days after symptom onset, plus at least 3 additional days without symptoms for symptomatic patients.
- 10 days after positive test for SARS-CoV-2 for asymptomatic cases.

However, several countries, (e.g. Italy), continue to apply the earlier testing criteria including a negative PCR test, which can result in individual being kept in isolation for several weeks or even months.

Recommended quarantine period for contacts and for travelers has not changed and remains set at 14 days.

Contact tracing can be effective in reducing the risk of spread of the virus (Keeling 2020) but is a complex and resource intensive exercise. It is most effective when implemented early in the outbreak, before there is sustained community transmission. Once cases are soaring, identifying and monitoring all the potential contacts using only the public health resources becomes close to impossible and additional measures like physical distancing, face masks and localized lockdowns become necessary (Cheng 2020). WHO has published detailed guidance on contact tracing for COVID-19 and alternative approaches to contact tracing that results in resource-saving measures have recently been suggested. (ECDC, April 2020)

As stated by several authors, (Steinbrook, 2020, Salathé 2020) in countries that have managed to bring the pandemic under control a necessary step in “reopening” society is to have sufficient testing and contact tracing capacities to successfully contain the outbreaks that will inevitably occur as social restrictions are removed or relaxed. The coming winter months will show which countries will have learned this important lesson.
Tracking apps

Mobile phone data reveal astonishing details about population movements. According to an analysis by Orange, a French phone operator, data from its telephone subscribers revealed that 17% of the inhabitants of Grand Paris (Métropole du Grand Paris, 7 million people) left the region between March 13 and 20 – just before and after the implementation of the French lockdown measures (Le Monde, 4 April 2020). Again, mobile phone data from individuals leaving or transiting through the prefecture of Wuhan between 1 January and 24 January 2020 showed that the distribution of population outflow from Wuhan accurately predicted the relative frequency and geographical distribution of SARS-CoV-2 infections throughout China until 19 February 2020 (Jia JS 2020).

Numerous countries have tried to harness the power of the smartphone to design and target measures to contain the spread of the pandemic (Oliver 2020). In addition to the dissemination of COVID-19 information and prevention messages, the use of smartphones in support to contact tracing has been promoted widely. This contact tracing system (better named “exposure notification”) would basically use an application to detect if the phone has come in close distance from another phone of a person diagnosed with SARS-COV-2 and potentially infectious. It will then give a warning message prompting the owner to seek medical assistance, self-isolation, and testing.

The deployment of these tracking applications has faced several hurdles, including the need for inter-operability across platforms (Google, Apple) and across countries (unfortunately, each European country has developed its own app); the possibility of false-positive alerts; and the need for a majority of the population to download and regularly activate the app to be truly effective. The need to preserve the privacy of the users forced less performing technical solutions (e.g. decentralized data systems with data only stored in each phone vs centralized database; preference for less-accurate Bluetooth connection over GPS geo-localization; voluntary decision required on the sharing of data; ensuring time-limited storage of collected data, etc.) For example, in June, Norway’s health authority had to delete all data gathered via its Covid-19 contact-tracing app and suspend its further use following a ruling by the Norwegian Data Protection Authority.

A few months into their introductions, most COVID-19 tracking apps have failed to deliver as expected. In almost all countries only a small proportion of the population have downloaded the app (only Qatar, Israel, Australia, Switzerland, and Turkey have seen downloads above the minimum threshold of 15% of the population) and probably even less people are regularly activating it. More importantly, the success of a tracking application should not be
measured by the number of downloads but by the number of contacts detected, which so far have been relatively few (due to privacy concerns, the total number of contacts is not available in countries where information is decentralized).

Maybe, with additional improvements, these tracking applications will become more efficient and effective in future, though they will probably only be only a support rather that a replacement for a traditional “manual” contact tracing system.

**Mandatory use of face masks**

Wearing a face mask to protect self and others from SARS-COV-2 infection may be an individual choice (see above). However, as of 6 May 2020, more than 120 countries have made wearing a mask in some settings a mandatory requirement as a collective preventive public health measure. Mandatory settings range from “everywhere in public” to all indoor public places, public transportation, shops, workplaces, schools, etc. Children and people with breathing difficulties are often exempted from the mandatory use of face masks. (US CDC 2020, WHO 2020, ECDC 2020) As a result, the global number of people regularly wearing masks in public has soared, reaching the peak of 80-90% of the population in most countries in Asia but also in Italy, France, and Spain. Surprisingly, mask acceptance has increased to the point of being branded as a fashion items.

As shown in the chart, authorities in Asia have mandated the use of face masks in public at the early stages of the pandemic, which contributed to reduced spread and the sharp drops in infections. As mentioned earlier, in many other parts of the world, conflicting advice with misleading or incomplete information about the usefulness of masks has caused confusion among the population and a late adoption of this preventive measure. In addition, a growing “no-Masks” movement has gathered momentum, staging rallies in several countries. Regardless, as new infections have started to increase again following the summer reopening, mandatory mask requirements are being introduced again in many European countries and becoming a norm in most public places.
Ban on mass gatherings

Recognizing their potential role in generating explosive clusters of SARS-COV-2 infections, (McCloskey 2020, Ebrahim 2020) most countries have implemented nationwide bans of mass gathering like sporting and cultural events, concerts, religious celebrations, rallies and political demonstrations, etc. Several important international mass gatherings events have been cancelled or postponed, including the Tokyo 2020 Olympic Games, Euro 2020 football championship, Formula 1 Grand Prix races, the Eurovision Song Contest 2020, 2020 Geneva Motor Show, Christian Holy Week events in Rome, Umrah pilgrimage to Mecca, and many others.

It is currently uncertain under which conditions cultural events that require closeness of spectators (e.g. cinema, theatre, opera, etc.), religious ceremonies, political rallies, and other social events that require the contemporaneous presence of large numbers of clients in a restricted, closed space (discos, bar, etc.) can be resumed without the risk of resulting in a super spreader event. The limited reopening of these premises during the summer holidays has recently been associated with a resurgence of the spread of the virus ob-
served in Greece, Spain, France, and Italy. Most sport events have resumed, but without public. WHO has recently published key recommendations for mass gatherings in the context of COVID-19. Unless the risk of SARS-COV-2 spread is reduced significantly, postponing or cancelling of planned large event is likely to continue in the months to come.

**Localized and nationwide Lockdowns**

Lockdowns (or “stay-at-home orders”) are restrictions of movements of the whole population, ordered by a government authority to suppress or mitigate an epidemic or pandemic. They differ from quarantine in that all residents are supposed to stay at home, except for those involved in essential tasks, while quarantine is usually limited to people suspected to be infected.

Lockdowns and social distancing have been used for centuries in the fight against epidemics, as famously illustrated in the Decameron, a book by Boccaccio, an Italian writer, which contains tales told by a group of young people sheltering in a villa outside Florence to escape the Black Death of 1348. However, the 2020 nationwide lockdowns which ordered almost 4 billion people in 90 countries to stay at home were unprecedented in human history. (see also Chronology) For the first time, lockdowns were imposed initially in a whole city of 10 million people (Wuhan), then to 60 million people in the whole province of Hubei, finally to a whole country (Italy, followed by most other European countries.) Though countries opted for more (China) or less (Europe) strict confinement measures, lockdowns were clearly effective in decreasing a hypothesized infection rate of 60% to 70% to less than 10%. (Cowling 2020)

How strict such measures can be has been shown in Hong Kong (Normile 2020). The recipe: hospitalize all those who test positive, regardless of whether they have symptoms, order two weeks of self-quarantine to all close contacts, introduce electronic wristbands, etc. A website even displays the location of infected people in Hong Kong at all times: https://chp-dashboard.geodata.gov.hk/covid-19/en.html. Such strict measures can be very effective but would not be acceptable or feasible in most countries. Indeed, one of the limitations of lockdowns is that they can never be 100% complete. People occupied in essential services (e.g. health, security, transport, communication, food production and delivery, etc.) will need to be allowed to move and work, and sick people will need to continue to access health services.

Generalized lockdowns are blunt prevention tools, affecting the whole healthy population to reduce the risk of transmission from the relatively few
potentially infectious individuals. (Hsiang 2020) They impose a major economic and social burden on the affected populations, while also preventing at times access to prevention and treatment for other health conditions (Charlesworth 2020). Various authors (Marshall 2020, Pierce 2020, Williams 2020, Galea 2020) have emphasized the combined impact of the pandemic, social distancing and closures on the mental health of the population. In addition, implementing generalized lockdowns in low-income countries is particularly difficult. People in the informal economy without social net benefits would be forced to choose between the risk of infection and risking of falling into poverty and hunger. (ILO, 2020)

In fact, widespread testing, isolation and quarantine, combined with population behavioral changes (physical distancing, use of masks, hand hygiene) – that have a less disruptive social and economic impact – have been shown to meaningfully contain COVID-19 if applied widely and consistently (Cowling 2020). A key metric for their success is whether critical care capacities are exceeded or prolonged or whether intermittent social distancing will be necessary into 2022 (Kissler 2020).

In summary, the tighter you control the infected and trace and isolate the close contacts, the less restriction you will have to impose on the uninfected. Hopefully countries will have learnt the lesson and, being better prepared, will be able to avoid in future the need for generalized lockdowns to respond to COVID-19 (and other epidemics). However, until an effective vaccine becomes available, localized temporary lockdowns might still be required in the fight against this pandemic.

**Travel bans/border closures**

It has been long recognized that both land, sea and air travel can be efficient and rapid routes for the international spread of a pandemic virus. (Hufnagel 2004, Hollingsworth 2007) The conditions for restricting movements of people and goods between countries in case of a public health emergency are therefore regulated by the WHO International Health Regulations adopted by all WHO member states in 2005 (IHR 2005).

As of 18 June 2020, almost all (191) countries have taken some measures that restrict people’s movement since the COVID-19 pandemic began. Measures range from control of entry onto the territory of a State to control of movement within a territory, comprising of partial or total border closures (161 countries) and international flight suspensions (154 countries).

As pointed out by some authors (Habibi 2020), these measures are in breach of the IHR 2005, as they do not seem grounded on “scientific principles, scien-
tific evidence, or advice from WHO” as required by IHR. (WHO 2005) This position is based on several scientific studies that have shown how the imposition of travel bans and border closures can be only partially effective in slowing down the introduction and spread of an epidemic or pandemic virus (like influenza or Ebola) while being potentially damaging and even counterproductive. (Brownstein 2006, Mateus 2014, Poletto 2014)

In fact, widespread travel restrictions and border closures have not prevented SARS-COV-2 from reaching quickly just about every country on the planet (see section on Epidemiology). Though Italy was the first in Europe to impose a travel ban on China, it was also the first European country to experience a major COVID-19 outbreak. Australia has imposed a total travel ban since 24 March that contributed initially to stop the spread of the virus but did not prevent returning citizens and poorly-trained quarantine guards to break the rules and cause the ongoing major outbreak in Melbourne. One reason why travel bans are usually ineffective is that you cannot prevent everybody from entering a country. Some people (e.g. Citizens, long-term residents, diplomats, air or ship crews, health personnel, sometimes businessmen, etc.) are often exempted and able to travel under national or international agreements. Others (e.g. illegal migrants) can cross borders unofficially.

Some authors have also pointed out how the travel bans and border closures can restrict the movement of vital health equipment and supplies (e.g. medicines, PPEs, testing reagents and equipment) and also essential personnel, particularly needed in countries with limited resources (Devi 2020). Others suggest that early detection, hand washing, self-isolation, and household quarantine will likely be more effective than travel restrictions at mitigating this pandemic. (Chinazzi 2020)

On the other hand, the economic damage of travel bans has been substantial. The activities of airlines, airports, travel agents, hotels and resorts has basically come to a halt at the peak of the pandemic. Eurocontrol has recorded a 90% drop in air passenger in Europe at the end of April; the figure has improved with the reopening of borders but is still at -50% compared to 2019 as of mid-July. In May, the UN World Tourism Organization (UNWTO) projected the potential economic loss for the tourist industry worldwide at US$ 910 billion to US$ 1.2 trillion, with 100-120 million jobs at risk.

Like generalized lockdowns, generalized travel bans and border closures are blunt tools and can result in an erroneous and dangerous false sense of security in the population and in the authorities. While they might be partially effective in at least slowing down the introduction of a pathogen, they will eventually end up being breached one way or the other. Their impact on the life of many people, the economy and the trade is substantial and strict.
screening and quarantine measures can be as effective in avoiding transmission of the virus by imported cases. Most likely, as countries will increasingly learn how to deal with the risk of COVID-19 in more efficient and effective ways, international travel will finally be allowed to resume in a safe environment.

**Vaccinate for seasonal influenza and (hopefully soon) for COVID-19**

Several authors (Richmond 2020, Jaklevic 2020, Singer 2020, Rubin 2020, Maltezoua 2020) and public health agencies are recommending expanding seasonal flu vaccination in the context of the COVID-19 pandemic. This follows concerns about the potential “double epidemic” of COVID-19 and seasonal flu during the winter months (Balakrishnan 2020, Gostin 2020). There are indeed many similarities (but also a few important differences) between the two diseases (Solomon 2020, Zayet 2020, Faury 2020) which may complicate the differential diagnosis for symptomatic patients, e.g. similar transmission routes, similar symptoms for mild cases (except for signs of neurological involvement like anosmia), similar high-risk groups for severe complications and mortality. A “double epidemic” could overburden both primary care services and hospitals, require a major increase in diagnostic capacities, lead to unnecessary isolation and quarantine of influenza cases and even increase stigma and discrimination of anyone presenting with symptoms of a respiratory infection (Rubin 2020). The possibility of COVID-19 and flu co-infection should also not be ruled out (Kim 2020). Combined SARS-CoV-2 and flu diagnostic tests, as recently approved by the FDA and being evaluated in some countries in Europe, could be useful in quickly identifying the pathogen(s) involved from a single sample.

Increasing coverage of seasonal influenza vaccination among high-risk groups is a good public health measure on its own, as influenza is estimated to cause close to 10 million hospitalizations and between 294,000 and 518,000 deaths every year (Paget 2019, CDC-US). It is also an essential measure with COVID-19 to avoid a potential breakdown of health care systems and the related increase in mortality and morbidity. Unfortunately, the normal uptake of flu vaccination in high-risk groups (> 65 years of age) has been largely insufficient, averaging around 50% in OECD countries. Along with efforts to increase coverage in the recommended risk groups, additional measures being suggested include reducing the recommended age for vaccination from 65 to 60 years, universal vaccination of children aged 6 months to 17 years, mandatory vaccination for all health-care workers, including all workers and visitors of long-term care facilities (Balakrishnan 2020, Gostin 2020, CDC).
However, widespread implementation of these additional measures will not be simple. The usual misguided concerns about the safety of vaccines and more recent social media fake news reports about the possibility of flu vaccine causing COVID-19 will need to be addressed. Possible reduced healthcare seeking behaviors due to fear of SARS-CoV-2 infection could also be a challenge. In addition, despite efforts by vaccine manufacturers and a major increase in flu vaccine production capacities in the last decade due in part to preparation for a possible flu pandemic (Rockman 2020), vaccine availability is unlikely to be sufficient to meet such an increase in demand, at least for the coming northern hemisphere flu season in 2020-21.

The definition of the composition of the seasonal flu vaccine is agreed by a WHO advisory group of flu experts based on an analysis of the data generated by the WHO Global Influenza Surveillance and Response System (GISRS). The group reviews the results of flu surveillance, laboratory and clinical studies and makes recommendations on the composition of the influenza vaccine based on the best match with available vaccine viruses. The advisory group meetings are held in February (for the northern hemisphere’s seasonal influenza vaccine) and in September (for the southern hemisphere’s vaccine) to allow sufficient time (7-9 months) for the production of the required doses of vaccine. (Dunning 2020).

Influenza vaccine effectiveness can vary from season to season depending on the similarity or “match” between the flu vaccine and the flu viruses actually spreading in the community. During those years when the flu vaccine is not well matched to circulating influenza viruses, effectiveness can be as low as 20%, rising to 60% for the years when there is a good match between the flu vaccine and circulating viruses. However, even less effective influenza vaccines have been shown to reduce considerably the burden of severe cases of influenza, admission to ICUs, and flu-related deaths (Thompson 2018, Ferdinands 2019).

Several recent studies have reported that indicators of influenza activity have been declining substantially in 2020 in both the northern (e.g. in Asia and the US) and the southern hemispheres, including in countries that implemented limited lockdown measures (Soo 2020, Olsen 2020, Itaya 2020). The decreased influenza activity was closely associated with the introduction of interventions to reduce SARS-CoV-2 transmission. (Choe 2020). This is really good news, as the evidence on the effectiveness of public health interventions in slowing the spread of a pandemic virus has been otherwise limited (Fong 2020, Xiao 2020, Ryu 2020). If these findings are confirmed during the coming winter season in the northern hemisphere, not only this would avoid the danger of a “dual epidemic” but it will also underscore that non-
pharmaceutical interventions are essential in the response to future pandemics and could become standard interventions, in addition to vaccination, for reducing the health burden of seasonal influenza and other respiratory infections in high risk groups.

On the down side, the limited detection and isolation of flu viruses by the WHO surveillance system will reduce the availability of updated and robust data for the decision on the composition of the flu vaccine for 2021, raising the danger of a poor match between future influenza vaccines and circulating flu viruses.

Additional potential good news could come from research on the effects of influenza vaccination on the severity of SARS-CoV-2 infection. Among the few studies available, a recently pre-published paper (Fink 2020) reports on the analysis of data from 92,664 confirmed COVID-19 cases in Brazil showing that patients who received a trivalent influenza vaccine during the last campaign (March 2020) experienced on average 8% lower odds of needing intensive care treatment (95% CIs [0.86, 0.99]), 18% lower odds of requiring invasive respiratory support (0.74, 0.88) and 17% lower odds of death (0.75, 0.89). Similar conclusions were reached in another pre-print paper modelling COVID-19 mor-
tality data and recent influenza vaccination coverage in the US (Zanettini 2020).

More studies are clearly required before reaching conclusions, but the available evidence does suggest that increasing coverage of influenza vaccination would result in both direct and indirect benefits in terms of reduced morbidity and mortality from both COVID-19 and influenza. These efforts could also have long-term benefits in expanding influenza vaccine production and uptake, both for seasonal influenza and in preparation for future flu pandemics. Experience and lessons learned from these efforts will be of great value once a COVID-19 vaccine becomes available, since production, distribution and promotion of uptake for the new vaccine will face similar challenges and will need to prioritize the same vulnerable populations (Jaklevic 2020, Mendelson 2020).

Containment or mitigation of COVID-19?

Public health interventions to control an outbreak or an epidemic aim at achieving two separate but linked objectives (Zhang 2020, OECD 2020):

- To contain the spread by minimizing the risk of transmission from infected to non-infected individuals, eventually suppressing transmission and ending the outbreak.
- To mitigate the impact by slowing the spread of the disease while protecting those at higher risk. While not halting the outbreak, this would “flatten the epidemic curve”, reduce disease burden and avoid a peak in health care demand. In case of new emerging pathogens, it would also buy time to develop effective treatments or vaccines. (Djidjou-Demasse 2020)

Containment strategies rely heavily on case detection and contract tracing, isolation, and quarantine. They are usually applied most successfully in the early stages of an outbreak or epidemic, when the number of cases is still manageable by the public health system. (Hellewell 2020) When containment measures are insufficient or applied too late, mitigation becomes the only option, usually through the imposition of generalized preventive measures like closing of non-essential activities, social distancing, mandatory mask use, or lockdowns. (Parodi 2020, Walker 2020)

During the first months of the COVID-19 pandemic, several countries (China, Vietnam, South Korea, Australia, New Zealand) have shown how the implementation of a well-timed, comprehensive package of aggressive containment and mitigation policies can be effective in suppressing the COVID-19 epidem-
ic, at least in the short-term. Other countries (most countries in Europe), have not been able to suppress transmission but have managed to mitigate the impact and bring the spread of SARS-COV-2 down to acceptable levels, while in others the pandemic is still raging with no end in sight (e.g., US, Brazil, most of Latin America.) However, as long as the virus is actively spreading anywhere in the world, no country can feel safe (as shown by the recent outbreaks in Victoria, Australia and in New Zealand).

Conclusion

While the quest for an effective vaccine or antiviral treatment continues, countries are still struggling to find the right mix of preventive measures (and the right balance between health and socio-economic priorities) to build an effective response to the COVID-19 pandemic.

Finding the right prevention mix means identifying what are the most cost-effective measures that can be widely implemented to reduce or halt the transmission of the virus. For this, we need a better understanding of how this virus spreads and how effective the different preventive measures are. Only more research and better science will provide this information.

However, finding the right balance also means recognizing that some measures can be effective, but at a very high social, economic, political, educational, and even health costs. These are political decisions. For example, it is unlikely that many European countries will accept to impose again strict generalized lockdowns, border closures or travel bans. These measures are simply too costly for society to be acceptable.

The most likely scenario is that to respond to new cluster of cases or the acceleration of the spread of the virus, perhaps due to “superspreaders” events or a relaxation of individual preventive measures, localized time-limited public health measures will need to be imposed, their effectiveness judged by better monitoring of the spread of the virus. It is not ideal, it is not being “back to normal”, but in the absence of a “silver bullet” it is probably the best option we have right now to contain this pandemic.

References

Prevention at the personal level

Good respiratory hygiene/cough etiquette.

Face masks


- Renyi Zhang, View ORCID ProfileYixin Li, Annie L. Zhang, View ORCID ProfileYuan Wang, and Mario J. Molina Identifying airborne transmission as the dominant route for the spread of COVID-19 PNAS June 30, 2020 117 (26) 14857-14863; first published June 11, 2020 https://doi.org/10.1073/pnas.2009637117


- WHO Advice on the use of masks in the context of COVID-19, Interim guidance, 5 June 2020
Hand Hygiene


- Charles W. Schmidt **Lack of Handwashing Access: A Widespread Deficiency in the Age of COVID-19** Environmental Health Perspectives 2020 128:6 CID: 064002 [https://doi.org/10.1289/EHP7493](https://doi.org/10.1289/EHP7493)

- Kevin P Fennelly, MD **Particle sizes of infectious aerosols: implications for infection control** Lancet Respir Med 2020Published OnlineJuly 24, 2020 [https://doi.org/10.1016/S2213-2600(20)30323-](https://doi.org/10.1016/S2213-2600(20)30323-)

- WHO Interim recommendations on obligatory hand hygiene against transmission of COVID-19. 1 April 2020

- Guide to Local Production: WHO-recommended Handrub Formulations

Physical/Social distancing and avoiding crowded conditions


• Nazrul Islam, Stephen J Sharp, Gerardo Chowell, Sharmin Shabnam, Ichiro Kawachi, Ben Lacey, Joseph M Massaro, Ralph B D’Agostino Sr, Martin White. Physical distancing interventions and incidence of coronavirus disease 2019: natural experiment in 149 countries BMJ 2020; 370 doi: https://doi.org/10.1136/bmj.m2743 (Published 15 July 2020)

• Zeshan Qureshi, Nicholas Jones, Robert Temple, Jessica PJ Larwood, Trisha Greenhalgh, Lydia Bourouiba. What is the evidence to support the 2-metre social distancing rule to reduce COVID-19 transmission? CEBM, Published Online June 22, 2020


Speak quietly, don’t shout (or sing)!


Household hygiene

• Alex W H Chin; Julie T S Chu; Mahen R A Perera; Kenrie P Y Hui; Hui-Ling Yen; Michael C W Chan; et al. **Stability of SARS-CoV-2 in different environmental conditions** Lancet 2020:April 02, 2020DOI: https://doi.org/10.1016/S2666-5247(20)30003-3

• Radhika Gharpure; Candis M. Hunter; Amy H. Schnall; Catherine E. Barrett; Amy E. Kirby; Jasen Kunz; Kirsten Berling; Jeffrey W. Mercante; Jennifer L. Murphy; Amanda G. Garcia-Williams. **Knowledge and Practices Regarding Safe Household Cleaning and Disinfection for COVID-19 Prevention** — United States, MMWR Morb Mortal Wkly Rep. May 2020 Early Release / June 5, 2020 / 69 https://www.cdc.gov/mmwr/volumes/69/wr/mm6923e2.htm?s_cid=mm6923e2_w


**Chemoprophylaxis**

Post exposure prophylaxis (PEP) with antiviral drugs after documented exposure can reduce the risk of infection. In the future, SARS-CoV-2-PEP could be used to reduce viral shedding in suspected cases and as a prophylactic treatment of contacts.

**Prevention at the community/societal levels**

**Widespread testing, quarantine and intensive contact tracing**


https://doi.org/10.3201/eid2610.201315

• Contact tracing for COVID-19: current evidence, options for scale-up and an assessment of resources needed. ECDC, April 2020


Quarantine and isolation of suspected or confirmed cases


• **Criteria for releasing COVID-19 patients from isolation** WHO Scientific Brief, 17 June 2020
https://www.who.int/publications/i/item/criteria-for-releasing-covid-19-patients-from-isolation

• Muge Cevik, Matthew Tate, Oliver Lloyd, Alberto Enrico Maraolo, Jenna Schafers, Antonia Ho SARS-CoV-2, SARS-CoV-1 and MERS-CoV viral load dynamics, duration of viral shedding and infectiousness: a living systematic review and meta-analysis medRxiv 2020.07.25.20162107; doi: https://doi.org/10.1101/2020.07.25.20162107

Test. Treat. Track.

• **Contact tracing in the context of COVID-19: Interim guidance**, WHO 10 May 2020


Tracking apps


• Mobile phone data for informing public health actions across the COVID-19 pandemic life cycle By Nuria Oliver, Bruno Lepri, Harald Sterly, Renaud Lambiotte, Sébastien Deletaille, Marco De Nadai, Emmanuel Letouzé, Albert Ali Salah, Richard Benjamins, Ciro Cattuto,
Vittoria Colizza, Nicolas de Cordes, Samuel P. Fraiberger, Till Koebe, Sune Lehmann, Juan Murillo, Alex Pentland, Phuong N Pham, Frédéric Pivetta, Jari Saramäki, Samuel V. Scarpino, Michele Tizzoni, Stefaan Verhulst, Patrick Vinck Science Advances05 Jun 2020 : eabc0764


**Mandatory face masks**

- **Recommendation Regarding the Use of Cloth Face Coverings, Especially in Areas of Significant Community-Based Transmission**, US CDC 2020

- **Considerations for Wearing Masks. Help Slow the Spread of COVID-19.** US CDC, July 2020

- **WHO Advice on the use of masks in the context of COVID-19, Interim guidance, 5 June 2020**

- **European Centre for Disease Prevention and Control. Using face masks in the community.** Stockholm: ECDC; 2020

**Ban on mass gatherings**


- **Key planning recommendations for mass gatherings in the context of the current COVID-19 outbreak**, WHO Interim guidance 29 May 2020 https://www.who.int/publications/i/item/10665-332235
Localized and nationwide Lockdowns


Travel bans/border closures


- #COVID19 Government Measures Dataset, ACAPS, 2020


- Updated WHO recommendations for international traffic in relation to COVID-19 outbreak, WHO 29 February 2020


• https://www.weforum.org/agenda/2020/04/covid19-airports-pandemics-public-health/

Vaccinate for seasonal influenza and for COVID-19 (not yet available)


• Jaklevic MC. Flu Vaccination Urged During COVID-19 Pandemic. JAMA. 2020 Sep 8;324(10):926-927. PubMed:


• Choe YJ, Lee JK. The Impact of Social Distancing on the Transmission of Influenza Virus, South Korea, 2020. Osong Public Health


• Guenther Fink, Nina Orlova-Fink, Tobias Schindler, Sandra Grisi, Ana Paula Ferrer, Claudia Daubenberger, Alexandr Brentani Inactivated trivalent influenza vaccine is associated with lower mortality among Covid-19 patients in Brazil medRxiv 2020.06.29.20142505- Full-text: https://doi.org/10.1101/2020.06.29.20142505


Containment and mitigaton of COVID-19


Environmental hygiene and disinfection

• Cleaning and disinfection of environmental surfaces in the context of COVID-19, WHO 16 May 2020


• Disinfection of environments in healthcare and non-healthcare settings potentially contaminated with SARS-CoV-2, ECDC, March 2020

Hospitals and other health care settings

- US CDC Interim Infection Prevention and Control Recommendations for Patients with Suspected or Confirmed Coronavirus Disease 2019 (COVID-19) in Healthcare Settings (Update May 18, 2020)

Nursing facilities

Long-term Care Institutions
Workplaces

- Prevention and Mitigation of COVID-19 at Work ACTION CHECKLIST, International Labor Organization 16 April 2020

Schools

- UK Department of Education Guidance Actions for schools during the coronavirus outbreak Updated 3 June 2020

Prisons


**Homeless shelters**

4. Virology

Emilia Wilson
Wolfgang Preiser
5. Immunology

Thomas Kamradt
6. Diagnostic Tests and Procedures

Christian Hoffmann
7. Clinical Presentation

Christian Hoffmann
Bernd Sebastian Kamps
8. Treatment

Christian Hoffmann
9. Severe COVID

Markus Unnewehr
Peter Rupp
Matthias Richl
10. Comorbidities

Christian Hoffmann
11. Pediatrics

Tim Niehues
Jennifer Neubert

Acknowledgements: Without the skillful help of Andrea Groth (Helios Klinikum Krefeld), the preparation of this manuscript would not have been possible. We thank cand. med. Lars Dinkelbach (Heinrich Heine Universität Düsseldorf) for critically reading the manuscript.
12. The First Seven Months

Sunday, 1 December
According to a retrospective study published in The Lancet on 24 January 2020\(^1\), the earliest laboratory confirmed case of COVID-19 in Wuhan was in a man whose symptoms began on 1 December 2019. No epidemiological link could be found with other early cases. None of his family became ill.

Thursday, 12 December
In Wuhan, health officials start investigating a cluster of patients with viral pneumonia. They eventually find that most patients have visits to the Huanan Seafood Wholesale Market in common. The market is known for being a sales hub for poultry, bats, snakes, and other wildlife.

Monday, 30 December 2019
Li Wenliang (en.wikipedia.org/wiki/Li_Wenliang), a 34-year-old ophthalmologist from Wuhan, posts a message on a WeChat group alerting fellow doctors to a new disease at his hospital in late December. He writes that seven patients have symptoms similar to SARS and are in quarantine. Li asks his friends to inform their families and advises his colleagues to wear protective equipment.

Tuesday, 31 December 2019
The Wuhan police announce that they are investigating eight people for spreading rumors about a new infectious diseases outbreak (see 30 December).

The Wuhan Municipal Health Commission reports 27 patients with viral pneumonia and a history of exposure to the Huanan Seafood Wholesale Market. Seven patients are critically ill. The clinical manifestations of the cases were mainly fever, a few patients had difficulty breathing, and chest radiographs showed bilateral lung infiltrative lesions. The report says that the “disease is preventable and controllable”. WHO is informed about the outbreak.

---

\(^1\) Huang, Chaolin et al., Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China January 24, 2020 https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30183-5/fulltext#%20
Thursday, 1 January
The Huanan Seafood Wholesale Market is shut down.

Friday, 3 January
While examining bronchoalveolar lavage fluid collected from hospital patients between 24 and 29 December, Chinese scientists at the National Institute of Viral Disease Control and Prevention ruled out the infection with 26 common respiratory viruses, determined the genetic sequence of a novel β-genus coronaviruses (naming it '2019-nCoV') and identified three distinct strains.²

Li Wenliang is summoned to a local public security office in Wuhan for “spreading false rumours”. He is forced to sign a document where he admits having made “false comments” and “disrupted social order.” Li signs a statement agreeing not to discuss the disease further.

On the Weibo social network, Wuhan police say they have taken legal action against people who “published and shared rumors online”, “causing a negative impact on society”. The following day, the information is taken up by CCTV, the state television. CCTV does not specify that the eight people accused of “spreading false rumors” are doctors.

Sunday, 5 January
WHO issues an alert that 44 patients with pneumonia of unknown etiology have been reported by the national authorities in China. Of the 44 cases reported, 11 are severely ill while the remaining 33 patients are in stable condition. https://www.who.int/csr/don/05-january-2020-pneumonia-of-unknown-cause-china/en/

Tuesday, 7 January
Chinese officials announce that they have identified a new coronavirus (CoV) from patients in Wuhan (pre-published 17 days later: https://doi.org/10.1056/NEJMoa2001017). Coronaviruses are a group of viruses that cause diseases in mammals and birds. In humans, the most common coronaviruses (HCoV-229E, -NL63, -OC43, and -HKU1) continuously cir-


COVID Reference ENG 005
Coronaviruses circulate in the human population; they cause colds, sometimes associated with fever and sore throat, primarily in the winter and early spring seasons. Two coronavirus have also been responsible for human outbreaks of SARS and MERS. These viruses are spread by inhaling droplets generated when infected people cough or sneeze, or by touching a surface where these droplets land and then touching one’s face.

**Friday, 10 January**

The gene sequencing data of the new virus was posted on Virological.org by researchers from Fudan University, Shanghai. A further three sequences were posted to the Global Initiative on Sharing All Influenza Data (GISAID) portal.

On 10 January 2020, Li Wenliang, coronavirus whistleblower, started having symptoms of a dry cough. Two days later, Wenliang started having a fever and was admitted to the hospital on 14 January 2020. His parents also contracted the coronavirus and were admitted to the hospital with him. Wenliang tested negative several times until finally testing positive for the coronavirus on 30 January 2020.

**Sunday, 12 January**

Using the genetic sequence of the new coronavirus made available to WHO, laboratories in different countries start producing specific diagnostic PCR tests.

The Chinese government reports that there is no clear evidence that the virus passes easily from person to person.

**Monday, 13 January**

Thailand reports the first case outside of China, a woman who had arrived from Wuhan. Japan, Nepal, France, Australia, Malaysia, Singapore, South Korea, Vietnam, Taiwan, and South Korea report cases over the following 10 days.

**Tuesday, 14 January**

WHO tweeted that “preliminary investigations conducted by the Chinese authorities have found no clear evidence of human-to-human transmission of the novel coronavirus (2019-nCoV) identified in Wuhan, China”. On the same day, WHO’s Maria Van Kerkhove said that there had been “limited human-to-human transmission” of the coronavirus, mainly small clusters in families,
adding that “it is very clear right now that we have no sustained human-to-
human transmission”3

**Saturday, 18 January**

The Medical Literature Guide Amedeo (www.amedeo.com) draws the attention of 50,000+ subscribers to a study from Imperial College London, Estimating the potential total number of novel Coronavirus cases in Wuhan City, China, by Imai et al. The authors estimate that “a total of 1,723 cases of 2019-nCoV in Wuhan City (95% CI: 427 – 4,471) had onset of symptoms by 12th January 2020”. Officially, only 41 cases were reported by 16th January.

**Monday, 20 January**

China reports three deaths and more than 200 infections. Cases are now also diagnosed outside Hubei province (Beijing, Shanghai and Shenzhen). Asian countries begin to introduce mandatory screenings at airports of all arrivals from high-risk areas of China.

After two medical staff were infected in Guangdong, the investigation team from China’s National Health Commission confirmed for the first time that the coronavirus can be transmitted between humans.4

**Wednesday, 22 January 2020**

A WHO China office field mission to Wuhan issued a statement saying that there was evidence of human-to-human transmission in Wuhan, but more investigation was needed to understand the full extent of transmission.5

**Thursday, 23 January**

In a bold and unprecedented move, the Chinese government puts tens of millions of people in quarantine. Nothing comparable has ever been done in human history. Nobody knows how efficient it will be.

All events for the Lunar New Year (starting on January 25) are cancelled.

The WHO IHR (2005) Emergency Committee convened on 22–23 January acknowledged that human-to-human transmission was occurring with a preliminary R0 estimate of 1.4–2.5 and that 25% of confirmed cases were reported

---

5 https://www.who.int/china/news/detail/22-01-2020-field-visit-wuhan-china-jan-2020
to be severe. However, the Committee felt that transmission was limited and there was “no evidence” of the virus spreading at community level outside of China. Since the members could not reach a consensus, the committee decided that it was still too early to declare a Public Health Emergency of International Concern (PHEIC) and agreed to reconvene in approximately ten days’ time.  

A scientific preprint from the Wuhan institute of Virology, later published in Nature, announced that a bat virus with 96% similarity had been sequenced in a Yunnan cave in 2013. The sequence is posted the next day on public databases. It is confirmed that the novel coronavirus uses this same entry receptor as SARS-CoV.

Friday, 24 January

At least 830 cases have been diagnosed in nine countries: China, Japan, Thailand, South Korea, Singapore, Vietnam, Taiwan, Nepal, and the United States. The first confirmed evidence of human-to-human transmission outside of China was documented by the WHO in Vietnam. France reported its first three confirmed imported cases, the first occurrences in the EU.

Zhu et al. publish their comprehensive report about the isolation of a novel coronavirus which is different from both MERS-CoV and SARS-CoV (full-text: https://doi.org/10.1056/NEJMoa2001017). They describe sensitive assays to detect viral RNA in clinical specimens.

Huang et al. publish on The Lancet the clinical features of 41 patients (full-text: doi.org/10.1016/S0140-6736(20)30185-9). The report indicated the risk of contagious infection without forewarning signs during the incubation period and suggested a “pandemic potential” for the new virus.

---


Chan et al. describe a familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission (full-text: doi.org/10.1016/S0140-6736(20)30154-9).

Saturday, 25 January

The Chinese government imposes travel restrictions on more cities in Hubei. The number of people affected by the quarantine totals 56 million. Hong Kong declares an emergency. New Year celebrations are cancelled and links to mainland China restricted.

Monday, 27 January

In Germany, the first cluster of infections with person to person transmission from asymptomatic patients in Europe was reported. The source of infection was an individual from Shanghai visiting a company in Bavaria. She developed symptoms on the way back to China. Contacts at the company were tested and transmission was confirmed to asymptomatic contacts but also to people who had no direct contact with the index patient. Authors state that “The fact that asymptomatic persons are potential sources of 2019-nCoV infection may warrant a reassessment of transmission dynamics of the current outbreak.”

Tuesday, 28 January

WHO DG Dr. Tedros Adhanom Ghebreyesus met China President Xi Jinping in Beijing. They shared the latest information on the outbreak and reiterated their commitment to bring it under control. The WHO delegation highly appreciated the actions China has implemented in response to the outbreak, its speed in identifying the virus and openness to sharing information with WHO and other countries.

Thursday, 30 January


On the advice of the IHR Emergency Committee, WHO DG declared a Public Health Emergency of International Concern and advised “all countries should be prepared for containment, including active surveillance, early detection, isolation and case management, contact tracing and prevention of onward spread of 2019-nCoV infection, and to share full data with WHO.” WHO had received reports of 83 cases in 18 countries outside China and that there had been evidence of human-to-human transmission in 3 countries.

China reports 7,711 cases and 170 deaths. The virus has now spread to all Chinese provinces.

Giuseppe Conte, Italy’s Prime Minister, confirms the first two COVID-19 imported cases in Italy.

**Friday, 31 January**

Li Wenliang publishes his experience with Wuhan police station (see 3 January) with the letter of admonition on social media. His post goes viral.

India, the Philippines, Russia, Spain, Sweden, the United Kingdom, Australia, Canada, Japan, Singapore, the US, the UAE and Vietnam confirm their first cases.

**Sunday, 2 February**

The first death outside China, of a Chinese man from Wuhan, is reported in the Philippines. Two days later a death in Hong Kong is reported.

**Thursday, 6 February**


**Friday, 7 February**

Hong Kong introduces prison sentences for anyone breaching quarantine rules.

**Saturday, 8 February**

The French Health Minister confirmed that a cluster of 5 COVID-19 cases were detected in a ski resort in the French Alps. The index patient was a UK citizen who had traveled to Singapore on 20-23 January and then spent four days (24-
28 January) in a chalet in Contamines-Montjoie, in Haute-Savoie. He tested positive upon return to England. Four contacts in the same chalet tested positive, including a 9-year old boy who was attending a local school. None of the child’s contacts in school or at home became infected.

**Monday, 10 February**

Amedeo launches a weekly Coronavirus literature service which would later be called *Amedeo COVID-19*.

**Tuesday, 11 February**

Less than three weeks after introducing mass quarantine measures in China, the number of daily **reported cases starts dropping**.

The WHO announces that the new infectious disease would be called **COVID-19** *(Coronavirus disease 2019)* and that the new virus will be called **SARS-CoV-2**.

**Wednesday, 12 February**

On board the Diamond Princess **cruise ship** docked in Yokohama, Japan, 175 people are infected with the virus. Over the following days and weeks, almost 700 people will be infected onboard.

**Thursday, 13 February**

China changed the COVID-19 case definition to include clinical (radiological) diagnosis of patients without confirmatory test. As a result, Hubei reported 14,840 newly confirmed cases, nearly 10 times more than the previous day, while deaths more than doubled to 242. WHO indicated that for consistency it would report only the number of laboratory-confirmed cases.13

**Wednesday, 19 February**

Iran reports two deaths from the coronavirus.

At the San Siro stadium in Milan, the Atalanta soccer team from Bergamo wins the Champions League match against Valencia 4 to 1 in front of 44,000 fans from Italy (2,000 from Spain). The mass transport from Bergamo to Milan and return, hours of shouting as well as the following festivities in innumera-
ble bars have been considered by some observers as a coronavirus ‘biological bomb’.

**Thursday, 20 February**

A patient in his 30s tested positive for SARS-CoV-2 and was admitted to the intensive care unit (ICU) in **Codogno Hospital** (Lodi, Lombardy, Italy). The symptomatic patient had visited the hospital the day before but was not tested as he did not meet the suspected case epidemiological criteria (no link with China). His wife, 5 hospital staff, 3 patients and several contacts of the index patients also tested positive to the COVID-19. Over the next 24 hours, the number of reported cases would increase to 36, many without links to the Codogno patient or previously identified positive cases. A first COVID-19 death in a 78-year-old man was also reported. It is the beginning of the Italian epidemic. [jamanetwork.com/journals/jama/fullarticle/2763188](jamanetwork.com/journals/jama/fullarticle/2763188)

**Saturday, 22 February**

South Korea reports a sudden spike of 20 new cases of coronavirus infection, raising concerns about a potential “super spreader” who has already infected 14 people in a church in the south-eastern city of Daegu.

**Sunday, 23 February**

Italy confirms 73 new cases, bringing the total to 152, and a third death, making Italy the third country in the world by number of cases, after China and South Korea. A “red zone” area around Codogno is created, isolating 11 municipal areas. Schools are closed.

**Venice Carnival** is brought to an early close and sports events are suspended in the most-hit Italian regions.

**Monday, 24 February**

France, Bahrain, Iraq, Kuwait, Afghanistan and Oman report their first cases.

**Tuesday, 25 February**

A report of a joint WHO mission of 25 international and Chinese experts is presented to the public. The mission travelled to several different Chinese provinces. The most important findings are that the Chinese epidemic peaked and plateaued between the 23rd of January and the 2nd of February and declined steadily thereafter (Table 1).
This was the first sign that the aggressive use of quarantine ordered by the Chinese government was the right thing to do. Unfortunately, European countries which did not experience the SARS epidemic in 2003, would lose precious time before following the Chinese example.


Wednesday, 26 February

A president, fearing for his chances to be re-elected, downplays the threat from the coronavirus pandemic, twittering: “Low Ratings Fake News...are doing everything possible to make the Coronavirus [sic] look as bad as possible, including panicking markets, if possible.”

https://www.bmj.com/content/368/bmj.m941

Two days later, the same individual invokes magic: “It’s going to disappear. One day, it’s like a miracle, it will disappear.”

P.S. On 28 March, The Guardian would ask why this person failed the biggest test of his life.
Friday, 28 February
A quick look at European cases diagnosed outside of Italy from February 24-27 reveals that 31 of 54 people (57%) had recently travelled to Northern Italy. Epidemiologists immediately realize that an unusual situation is building up.

Saturday, 7 March
Official data show that China’s exports plunged 17.2 percent in the first two months of the year.

Sunday, 8 March
The Italian government led by Prime Minister Giuseppe Conte, deserves credit for instauing the first European lockdown, just two and a half weeks after the first autoctone Italian COVID-19 case was detected. First, strict quarantine measures are imposed on 16 million people in the state of Lombardy and 14 other areas in the north. Two days later, Conte would extend these to the entire country of 60 million people, declaring the Italian territory a “security zone”. All people are told to stay at home unless they need to go out for “valid work or family reasons”. Schools are closed.

Monday, 9 March
A president on Twitter: “So last year 37,000 Americans died from the common Flu. It averages between 27,000 and 70,000 per year. Nothing is shut down, life & the economy go on. At this moment there are 546 confirmed cases of CoronaVirus, with 22 deaths. Think about that!” (The Guardian)
Iran releases 70,000 prisoners because of the coronavirus outbreak in the country.

Tuesday, 10 March
Xi Jinping tours the city of Wuhan and claims a provisional victory in the battle against COVID-19. The last two of 16 temporary hospitals in the city are shut down.

Wednesday, 11 March
With more than 118,000 COVID-19 cases in 114 countries and 4,291 deaths, WHO DG declares the coronavirus outbreak a pandemic.
All schools in and around Madrid, from kindergartens to universities, are closed for two weeks.
Thursday, 12 March

Italy closes all shops except grocery stores and pharmacies.

In Spain, 70,000 people in Igualada (Barcelona region) and three other municipalities are quarantined for at least 14 days. This is the first time Spain adopts measures of isolation for entire municipalities.

Emmanuel Macron, the French president, announces the closure of nurseries, schools and universities from Monday, 16 March. He declares: “One principle guides us to define our actions, it guides us from the start to anticipate this crisis and then to manage it for several weeks, and it must continue to do so: it is confidence in science. It is to listen to those who know.” Some of his colleagues should have listened, too.

Friday, 13 March

The prime minister of an ex-EU country introduces the notion of ‘herd immunity’ as a solution to repeated future episodes of coronavirus epidemics. The shock treatment: accepting that 60% of the population will contract the virus, thus developing a collective immunity and avoiding future coronavirus epidemics. The figures are dire. With a little over 66 million inhabitants, some 40 million people would be infected, 4 to 6 million would become seriously ill, and 2 million would require intensive care. Around 400,000 Britons would die. The prime minister projects that “many more families are going to lose loved ones before their time.”

P.S. Five weeks later, The Guardian would still ask, “How did Britain get its coronavirus response so wrong?”

Saturday, 14 March

The Spanish government puts the whole country into lockdown, telling all people to stay home. Exceptions include buying food or medical supplies, going to hospital, going to work or other emergencies.

The French government announces the closure of all “non-essential” public places (bars, restaurants, cafes, cinemas, nightclubs) after midnight. Only food stores, pharmacies, banks, tobacconists, and petrol stations may remain open.

Sunday, 15 March

France calls 47 million voters to the poll. Both government and opposition leaders seem to be in favor of maintaining the municipal elections. Is this a textbook example of unacceptable interference of party politics with the
sound management of a deadly epidemic? Future historians will have to investigate.

**Monday, 16 March**

Ferguson et al. publish a new modelling study on likely UK and US outcomes during the COVID-19 pandemic. In the (unlikely) absence of any control measures or spontaneous changes in individual behaviour, the authors expect a peak in mortality (daily deaths) to occur after approximately 3 months. This would result in 81% of the US population, about 264 million people, contracting the disease. Of those, 2.2 million would die, including 4% to 8% of Americans over age 70. More important, by the second week in April, the demand for critical care beds would be 30 times greater than supply.

The model then analyzes two approaches: mitigation and suppression. In the mitigation scenario, SARS-CoV-2 continues to spread at a slow rate, avoiding a breakdown of hospital systems. In the suppression scenario, extreme social distancing measures and home quarantines would stop the spread of the virus. The study also offers an outlook at the time when strict “Stay at home” measures are lifted. The perspective is grim: the epidemic would bounce back.

**France** imposes strict confinement measures.

**Tuesday, 17 March**

Seven million people across the San Francisco Bay Area are instructed to “shelter in place” and are prohibited from leaving their homes except for “essential activities” (purchasing food, medicine, and other necessities). Most businesses are closed. The exceptions: grocery stores, pharmacies, restaurants (for takeout and delivery only), hospitals, gas stations, banks.

**Thursday, 19 March**

For the first time since the beginning of the coronavirus outbreak, there have been **no new cases in Wuhan** and in the Hubei province.

Californian Governor Gavin Newsom orders the entire population of California (40 million people) to “stay at home”. Residents can only leave their homes to meet basic needs like buying food, going to the pharmacy or to the doctor, visiting relatives, exercising.

**Friday, 20 March**

**Italy** reports 6,000 new cases and 627 deaths in 24 hours.

In **Spain**, the confinement due to the coronavirus reduces crime by 50%.
China reports no new local coronavirus cases for three consecutive days. Restrictions are eased, normal life resumes. The entire world now looks at China. Will the virus spread again?

The state of New York, now the center of the U.S. epidemic (population: 20 million), declares a general lockdown. Only essential businesses (grocers, restaurants with takeout or delivery, pharmacies, and laundromats) will remain open. Liquor stores? Essential business!

Sunday, 22 March

Byung-Chul Han publishes La emergencia viral y el mundo de mañana (El País): “Asian countries are managing this crisis better than the West. While there you work with data and masks, here you react late and borders are opened.”

Monday, 23 March

Finally, too late for many observers, the UK puts in place containment measures. They are less strict than those in Italy, Spain and France.

German Chancellor Angela Merkel self-quarantines after coming into contact with a person who tested positive for coronavirus.

Tuesday, 24 March

Off all reported cases in Spain, 12% are among health care workers.

The Tokyo Olympics are postponed until 2021.

India orders a nationwide lockdown. Globally, three billion people are now in lockdown.

Wednesday, 25 March

After weeks of stringent containment measures, Chinese authorities lift travel restrictions in Hubei province. In order to travel, residents will need the “Green Code” provided by a monitoring system that uses the AliPay app.

A 16-year-old girl dies in the south of Paris from COVID-19. The girl had no previous illnesses.

Thursday, 26 March

America First: the US is now the country with most known coronavirus cases in the world.
For fear of reactivating the epidemic, China bans most foreigners from entering the country.

**Friday, 27 March**

The Prime Minister and the Ministre of Health of an ex-EU country tests positive for coronavirus.

The Lancet publishes *COVID-19 and the NHS—"a national scandal".*

A paper by McMichael et al. describes a 33% case fatality rate for SARS-CoV-2 infected residents of a long-term care facility in King County, Washington, US.

**Sunday, 29 March**

The Guardian and the Boston Globe ask who might have blood on their hands in the current pandemic. The evolution of the US epidemic is being described as the worst intelligence failure in US history.

**Monday, 30 March**

Flaxman S et al. from the Imperial College COVID-19 Response Team publish new data on the possibly true number of infected people in 11 European countries. Their model suggests that as of 28 March, in Italy and Spain, 5.9 million and 7 million people could have been infected, respectively (see Table online). Germany, Austria, Denmark and Norway would have the lowest infection rates (proportion of the population infected). These data suggest that the mortality of COVID-19 infection in Italy could be in the range of 0.4% (0.16%-1.2%).

Moscow and Lagos (21 million inhabitants) go into lockdown.

The COVID-19 crisis causes some East European political leaders to consider legislation giving them extraordinary powers. In one case, a law was passed extending a state of emergency indefinitely.

SARS-CoV-2 is spreading aboard the aircraft carrier USS Theodore Roosevelt. The ship’s commanding officer, Captain Brett Crozier, sends an email to three admirals in his chain of command, recommending that he be given permission to evacuate all non-essential sailors, to quarantine known COVID-19 cases, and sanitize the ship. “We are not at war. Sailors do not need to die,” writes Crozier in his four-page memo. The letter leaks to the media and generates several headlines. Three days later, 2 April, Captain Crozier is sacked.

Later, testing of 94% of the crew of roughly 4,800 people would reveal around 600 sailors infected, a majority of whom, around 350, were asymptomatic.
April

Wednesday, 1 April

The United Nations chief warns that the coronavirus pandemic presents the world’s “worst crisis” since World War II.

Thursday, 2 April

Worldwide more than one million cases are reported. The true number is probably much higher (see the Flaxman paper on 30 March).

European newspapers run articles about why Germany has so few deaths from COVID-19.

Friday, 3 April

Some economists warn that unemployment could surpass the levels reached during the Great Depression in the 1930s. The good news: almost all governments rate saving tens or hundreds of thousands of lives higher than avoiding a massive economic recession. Has humanity become more human?

Le Monde, the most influential French newspaper, points to a more mundane side effect of the epidemic. As hairdressers are forbidden to work, colors and cuts will degrade. The newspaper predicts that “after two months, 90% of blondes will have disappeared from the face of the Earth”.

Saturday, 4 April

In Europe, there are signs of hope. In Italy, the number of people treated in intensive care units decreases for the first time since the beginning of the epidemic.

In France, 6,800 patients are treated in intensive care units. More than 500 of these have been evacuated to hospitals from epidemic hotspots like Alsace and the Greater Paris area to regions with fewer COVID-19 cases. Specially adapted TGV high-speed trains and aircraft have been employed.

Lombardy decides that as of Sunday 5 April, people must wear masks or scarves. Supermarkets must provide gloves and hydroalcoholic gel to their customers.

An Italian politician, less penetrable to scientific reasoning on a par with some of his colleagues in the US and Brazil, asks for churches to be open on Easter (12 April), declaring that “science alone is not enough: the good God is also needed”. Heureux les simples d’esprit, as the French would say.
Figure 2. Patients treated in intensive care units in Italy. For the first time since the beginning of the epidemic, the number decreases on 4 April. Source: Le Monde

Sunday, 5 April
The US surgeon general warns the country that it will face a “Pearl Harbor moment” in the next week.

US is the new epicenter of the COVID-19 epidemic. By the time of this writing (5 April), more than 300,000 cases and almost 10,000 deaths were reported. Almost half were reported from New York and New Jersey.

Tuesday, 7 April
Air quality improves over Italy, the UK and Germany, with falling levels of carbon dioxide and nitrogen dioxide. Will a retrospective analysis of the current lockdown reveal fewer cases of asthma, heart attacks and lung disease?

Wednesday, 8 April
Japan declares a state of emergency, Singapore orders a partial lockdown.

In Wuhan people are allowed to travel for the first time since the city was sealed off 76 days ago.

The Guardian publishes a well-documented timeline: “Coronavirus: 100 days that changed the world.”
Thursday, 9 April

EU finance ministers agree to a common emergency plan to limit the impact of the coronavirus pandemic on the European economy. The Eurogroup reaches a deal on a response plan worth more than €500 billion for countries hit hardest by the epidemic.

Passenger air travel has decreased by up to 95%. How many of the 700 airlines will survive the next few months? Will the current interruption of global air travel shape our future travel behaviors?

The epidemic is devastating the US economy. More than 16 million Americans have submitted unemployment claims in the past three weeks.

Friday, 10 April

COVID-19 treatment for one dollar a day? British, American and Australian researchers estimate that it could indeed cost only between 1 and 29 dollars per treatment and per patient.

Message from your mobile phone: “You have been in contact with someone positive for coronavirus.” Google and Apple announce that they are building a coronavirus tracking system into iOS and Android. The joint effort would enable the use of Bluetooth technology to establish a voluntary contact-tracing network. Official apps from public health authorities would get extensive access to data kept on phones that have been in close proximity with each other (George Orwell is turning over in his grave). If users report that they’ve been diagnosed with COVID-19, the system would alert people if they were in close contact with the infected person.

Spain discovers COVID Reference. Within 24 hours, more than 15,000 people download the PDF of the Spanish edition. The only explanation: a huge media platform displayed the link of our book. Does anyone know who did it?
Saturday, 11 April

More than 400 of 700 long-term care facilities (EHPAD in French, Etablissement d’Hébergement pour Personnes Agées Dépendantes) in the greater Paris region (pop. – 10 million) have COVID-19 cases.

In Italy, 110 doctors and about 30 other hospital workers have died from COVID-19, half of them nurses.

Sunday, 12 April

Easter 2020. Italy reports 361 new deaths, the lowest number in 25 days while Spain reports 603 deaths, down more than 30% from a high 10 days before.
The United Kingdom records its highest daily death toll of almost 1,000. The number of reported COVID-19-linked fatalities now exceeds 10,000. As in many other countries, the true numbers may be slightly higher due to underreporting of people dying in care homes.

The number of COVID-19-related deaths in the United States passes 22,000, while the number of cases tops 500,000. In New York there are signs that the pandemic could be nearing its peak.

**Monday, 13 April**

The COVID-19 pandemic exposes bad governance, not only in Brazil. The French newspaper *Le Monde* reveals the ingredients: denial of reality, search for a scapegoat, omnipresence in the media, eviction of discordant voices, political approach, isolationism and short-term vision in the face of the greatest health challenge in recent decades. The culprit?

Emmanuel Macron announces a **month-long extension to France’s lockdown**. Only on Monday, May 11, nurseries, primary and high schools would gradually reopen, but not higher education. Cafés, restaurants, hotels, cinemas and other leisure activities would continue to remain closed after May 11.

**Tuesday, 14 April**

**Austria** is the first European country to **relax lockdown measures**. It opens up car and bicycle workshops, car washes, shops for building materials, iron and wood, DIY and garden centers (regardless of size) as well as smaller dealers with a customer area under 400 square meters. These shops must ensure that there is only one customer per 20 square meters. In Vienna alone, 4,600 shops are allowed to open today. Opening times are limited to 7.40 a.m. to 7 p.m. The roadmap for the coming weeks and months:

- 1 May: All stores, shopping malls and hairdressers reopen (see also the April 3 entry, page 133).
- 15 May: Other services such as restaurants and hotels remain closed at least until mid-May.
- 15 May or later: Possible re-opening of classes in schools.
- July: possible – but improbable – organization of events of all sorts (sport, music, theater, cinema etc.).
There is a general obligation to wear a mask when shopping and on public transport.

The International Monetary Fund (IMF) forecasts a **contraction of 3% of the planet's GDP in 2020**. The possibility of an even more brutal fall in 2021 is not excluded. The possibly worst economic downturn since the Great Depression in 1929 will not spare any continent. In a recession like no other in peacetime for nearly a century, the countries of the eurozone, the United Kingdom and the United States might see a contraction in activity of between 5.9% and 7.5%. China’s economy is expected to grow by about 1%.

**US:** The CDC (Centers for Disease Control and Prevention) reports that more than 9,000 health care workers contracted COVID-19 as and at least 27 died. The median age was 42 years, and 73% were female. Deaths most frequently occurred in HCP aged ≥ 65 years.

**Wednesday, 15 April**

Philip Anfinrud and Valentyn Stadnytsky from the National Institutes of Health, Bethesda, report a laser light-scattering experiment in which speech-generated droplets and their trajectories were visualized. They find that when a test person says, “stay healthy,” numerous droplets ranging from 20 to 500 µm are generated. When the same phrase is uttered three times through a slightly damp washcloth over the speaker's mouth, the flash (droplet) count remains close to the background level. The video supports the recommendation of wearing face masks in public. The authors also found that the number of flashes (droplets) increased with the loudness of speech. The new message for billions of people caught in the COVID-19 epidemic: lower your voice!

**Friday, 17 April**

Luiz Inácio Lula da Silva, the former Brazilian president says that the current president is leading Brazil to “the slaughterhouse” with his irresponsible handling of coronavirus. In an interview with The Guardian, Lula says that Brazil’s “troglodyte” leader risks repeating the devastating scenes playing out in Ecuador where families have to dump their loved ones’ corpses in the streets.

On the **French aircraft carrier Charles-de-Gaulle**, a massive epidemic is. Among the 1760 sailors, 1,046 (59%) are positive for SARS-CoV-2, 500 (28%) present symptoms, 24 (1.3%) sailors are hospitalized, 8 on oxygen therapy and one in intensive care.
Saturday, 18 April

Chancellor Angela Merkel makes a television speech, her first in over 14 years in office. She describes the coronavirus crisis “as the greatest challenge since the Second World War” and exhorts the Germans: “It is serious. Take it seriously.”

Care England, Britain’s largest representative body for care homes, suggests that up to 7,500 residents may have died of COVID-19. This would be higher than the 1,400 deaths estimated by the government.

In Catalunya alone, some 6,615 hospital professionals and another 5,934 in old age care homes are also suspected of having or been diagnosed with COVID-19.

Sunday, 19 April

![Daily number of COVID-19 deaths](https://www.youtube.com/watch?v=lOVP2o3c4Gw)

Air traffic in Europe has plummeted more than 95% as nicely shown by this YouTube video by The Guardian: [https://www.youtube.com/watch?v=lOVP2o3c4Gw](https://www.youtube.com/watch?v=lOVP2o3c4Gw)

Monday, 20 April

For the first time in history, the West Texas Intermediate (WTI), the benchmark price for US oil, drops below $0. On certain specific contracts, it plunged down to minus 37 US dollars (-34 euros). After nearly two months of continuous collapse of the oil market, this paradoxical situation is the result of the COVID-19 pandemic which caused demand to fall by 30%. As oil wells contin-
Due to produce, there is no place to store the oil and investors are ready to pay to get rid of it.

Germany’s Oktoberfest is cancelled. The iconic beer festival, colloquially known as Die Wiesn or “the meadow”, attracts around 6 million visitors from around the world. It runs for more than two weeks (September/October) in packed tents with long wooden tables, where people celebrate traditional food, dancing, beer and clothing. The loss for the city of Munich is estimated to be around one billion euros.

**Tuesday, 21 April**

The Spanish newspaper El País publishes an intelligible overview of the battle between SARS-CoV-2 and the human body: “Así es la lucha entre el sistema inmune y el coronavirus.” ¡Fantástico!

Cancer Research UK reports that every week, 2,300 people with cancer symptoms are no longer examined. Screening examinations for breast and uterine cancer of over 200,000 women per week have been cancelled. According to The British Heart Foundation, 50 percent fewer people suspected of having a heart attack attended hospital emergency rooms in March. A 50% drop would be “equivalent to approximately 5000 of the expected people every month, or more than 1100 people every week, with possible heart attack symptoms not being seen in emergency departments.” Will we discover a hidden epidemic of COVID-19-related morbidity and mortality with millions of people dying not from coronavirus, but from other, actually treatable diseases?

**Thursday, 23 April**

Pandemic hilarity, as a president known for his poor science record stammers speculations about “injecting” “disinfectant” to cure COVID-19.

**Sunday, 26 April**

The city of Wuhan announces that all remaining COVID-19 cases have been discharged from the hospitals.

**Monday, 27 April**

Are genes determining coronavirus symptoms? After studying 2,633 identical and fraternal twins who were diagnosed with COVID-19, a group from King’s College London reports that COVID-19 symptoms appear to be 50% genetic
(fever, diarrhea, delirium and loss of taste and smell)\textsuperscript{14}. It is as yet unclear whether and to what extent reported deaths of identical twins can be attributed to genetic factors.

\textsuperscript{14} Williams FMK et al. Self-reported symptoms of covid-19 including symptoms most predictive of SARS-CoV-2 infection, are heritable. MedRxiv 27 April (accessed 8 May 2020). Abstract: https://www.medrxiv.org/content/10.1101/2020.04.22.20072124v2
May

Friday, 1 May
A new SARS-CoV-2 test could be able to identify virus carriers before they are infectious, according to a report by The Guardian. The blood-based test would be able to detect the virus’s presence as early as 24 hours after infection – before people show symptoms and several days before a carrier is considered capable of spreading it to other people.

Sunday 3 May
Roche gets US Food and Drug Administration emergency use approval for its antibody test, Elecsys Anti-SARS-CoV-2, which has a specificity rate of about 99.8% and a sensitivity rate of 100%.

Monday, 4 May
Italy is cautiously easing lockdown measures. People can go jogging but may not go to the beach; they may surf but now swim; and they can visit 6th grade relatives, but not friends, lovers or mistresses.

A French hospital that retested old samples from pneumonia patients discovers that it treated a man with the coronavirus as early as 27 December, a month before the French government confirmed its first cases.

Researchers from Bonn University, Germany, report a sero-epidemiological study of 919 people from Gangelt, a small German town which was exposed to a super-spreading event (carnival festivities). 15.5% were infected, with an estimated infection fatality rate of 0.36%. 22% of infected individuals were asymptomatic.

Tuesday, 5 May
Neil Ferguson, epidemiologist at the Imperial College, resigns his post as member of the British government’s Scientific Advisory Group for Emergences (SAGE) over an “error of judgement”. A newspaper had reported that he did not respect the rules of confinement (which he himself had contributed to establishing!) by receiving at least twice a 38-year-old woman at his home.

Anthony Fauci, the director of the United States National Institute of Allergy and Infectious Diseases, says that there is no scientific evidence to back the
theory that the coronavirus was made in a Chinese laboratory or leaked from a laboratory after being brought in from the wild (CGTN).

**Wednesday, 6 May**

The official COVID-19 death toll in the UK exceeds 30,000.

**Thursday, 7 May**

According to data released by the US Department of Labor, more than 33 million Americans have filed for initial jobless claims. This corresponds roughly to 21% of the March labor force.

Only 15 countries in the world have not officially reported a case of COVID-19 to WHO, namely: North Korea, Turkmenistan, Kiribati, Marshall Islands, Micronesia, Samoa, Salomon Island, Tonga, Tuvalu, Vanuatu, Cook Island, Nauru, Niue, Palau and Lesotho. (We know North Korea is cheating, and Turkmenistan and Lesotho cannot deny for long... It’s a true pandemic!)

According to figures by the [Office of National Statistics](https://www.ons.gov.uk), black people are more than four times more likely to die from COVID-19 than white people.

**Friday, 8 May 2020**

After pipedreams (German: Hirngespinste; French: élucubrations; Italian: visioni; Spanish: fantasías) about hydroxychloroquine and injecting disinfectants, today is the day where COVID-19 will “go away without vaccine”. The sad developments of the coronavirus pandemic have now accumulated sufficient evidence that the individual doesn’t believe himself what he is saying. The carefully timed and well-orchestrated ungrammatical utterings just obey one supreme life mission: continue staying in the news. Alas, there is an even more tragic aspect to the drama: Why on Earth do the world’s media insist on talking about this individual? Why can’t we read the news without seeing his face every single day? Why couldn’t we simply *totschweigen* him?

(Totschweigen is a superbly descriptive German verb: 1. tot dead; 2. schweigen to be silent; 3. totschweigen make someone dead silent – English: to hush up; French: passer sous silence; Italian: fare come se non esistesse; Portuguese: não falar em alguém.)

Today, we make a funereal promise: we’ll never talk about the individual again, not even on the day he dies.
Sunday, 10 May

Italians are looking on aghast at the UK’s coronavirus response, says The Guardian. Is it really no accident that Britain and America are the world’s biggest coronavirus losers?

Everything you always wanted to know about false negatives and false positives* (*but were afraid to ask) is now summarized in 10 steps to understand COVID-19 antibodies. The colors will help you memorize true and false negatives and positives.

Spain’s best newspaper El País publishes ‘ccu cccg cccg gca – The 12 letters that changed the world.’ (If you read Spanish, take a look.)

Monday, 11 May

France eases lockdown restrictions among a sense of incertainty. The newspaper Le Monde reports that according to official figures 8,674 new positive tests for SARS-CoV-2 were registered between May 1 and 9. Epidemiologist Daniel Lévy-Bruhl, head of the respiratory infections unit of Santé Publique France (Public Health France) estimates that the real figures are probably twice or three times as high (3,000 to 4,000 new infections each day) – despite barrier gestures, social distancing and general confinement.

Tuesday, 12 May

The MMWR publish a report about a high SARS-CoV-2 attack rate following exposure at a choir practice.

Wednesday, 13 May

There is evidence that China is censoring COVID Reference. Google Analytics data of two dozen websites, both medical (Amedeo, Free Medical Journals, FreeBooks4Doctors) and non-medical (TheWordBrain, Ear2Memory, GigaSardinian, GigaMartinique, SardoXSardi, Polish Yiddish and ItalianWithElisa, among others) show that by number of visitors, China was always among the Top 10 countries, generating between 3.3% and 14.8% of website traffic (see https://covidreference.com/censorship).

Not so with COVID Reference. Six weeks after the launch of COVID Reference, China is 27th, after Paraguay, accounting for 0.39% of global traffic. Is someone standing on the data line between COVID Reference and China (Figure 6)?

Kamps – Hoffmann
Figure 6. Google Analytics data for www.CovidReference.com on 13 May. Six weeks after the launch of COVID Reference, China is 27th, after Paraguay and right before the Netherlands and Russia.

Friday, 15 May

In a memorable blog entry for the British Medical Journal, Paul Garner, professor of infectious diseases at Liverpool School of Tropical Medicine, discusses his COVID-19 experience as having “been through a roller coaster of ill health, extreme emotions, and utter exhaustion”.

A video experiment using black light and a fluorescent substance demonstrates how quickly germs can be spread in environments such as restaurant buffets and cruise ships: www.youtube.com/watch?v=kGQEuuv9R6E.

Saturday, 16 May

A new highly transmissible and potentially deadly virus is detected in Germany: SADS, Severe Acute Dementia Syndrome. The new syndrome manifests as an irrepressible desire to ignore the danger of COVID-19. In several German cities, an improbable alliance takes to the streets – left- and right-wing extremists, antisemites, conspiracy theorists and anti-vaxxers –, claiming the right to live and to die without social distancing and face masks. The German Government immediately informs WHO.

Monday, 18 May

Merkel and Macron announce a 500,000 million euro aid plan for the reconstruction of Europe (El País).

Moderna announces that its experimental vaccine mRNA-1273 has generated antibodies in eight healthy volunteers ages 18 to 55. The levels of neutralizing antibodies matched or exceeded the levels found in patients who had recovered from SARS-CoV-2 infection (The Guardian).
**Wednesday, 20 May**

After an outbreak of coronavirus, Chinese authorities seal off the city of Shulan, a city of 700,000 close to Russian border, imposing measures similar to those used in Wuhan (The Guardian).

Google and Apple release their Exposure Notification System to notify users of coronavirus exposure: https://www.google.com/covid19/exposurenotifications.

We discover a website which shows where infected people in Hong Kong are at all times: https://chp-dashboard.geodata.gov.hk/covid-19/en.html (Figure 7). There is no doubt that the tighter you control the infected, the less restriction you have to impose on the uninfected. In Europe, strict measures such as those adopted in Hong Kong and South Korea are currently not compatible with existing legislation about privacy.

![Figure 7. Screenshot of the “Latest Situation of Coronavirus Disease (COVID-19) in Hong Kong”, https://chp-dashboard.geodata.gov.hk/covid-19/en.html.](image)

**Thursday, 21 May**

The Centers for Disease Control and Prevention (CDC) informs that rats rely on the food and waste generated by restaurants and other commercial establishments, the closures of which have led to food shortage among rodents, especially in dense commercial areas. CDC warns of unusual or aggressive rodent behavior.
Will SARS-CoV-2 seal the fate of the Airbus A380? Air France chooses to end the operations of the aircraft, judged to be too expensive, too polluting and not profitable enough (Le Monde).

**Friday, 22 May**

Zhu et al. publish *Safety, Tolerability, and Immunogenicity of a Recombinant Adenovirus type-5 Vectored COVID-19 Vaccine*.

Fafi-Kremer 2020 et al. pre-publish *Serologic responses to SARS-CoV-2 infection among hospital staff with mild disease in eastern France*, reporting that neutralizing antibodies against SARS-CoV-2 were detected in virtually all hospital staff (n=160) sampled from 13 days after the onset of COVID-19 symptoms (see also Le Monde).

**Saturday, 23 May**

In Lower Saxony, Germany, 50 people are in quarantine after an outbreak in a restaurant (Der Spiegel).

In Frankfurt, Germany, authorities report more than 40 people infected with SARS-CoV-2 after a religious service (Der Spiegel).

**Wednesday, 27 May**

Colombian designers prepare cardboard hospital beds that double as coffins (The Guardian).

Andrzej Krauze publishes a cartoon on the fallout from the COVID-19 pandemic.

**Sunday, 31 May**

More than 50 million people across the US could go hungry without help from food banks or other aid (Feeding America).
June

**Wednesday, 3 June**
In the hope of saving its tourist industry, Italy reopens its borders.

**Tuesday, 4 June**
The Lancet *makes one of the biggest retractions in modern history* (The Guardian).

**Friday, 5 June**
The chief investigators of the RECOVERY trial report that there is no clinical benefit from use of hydroxychloroquine in hospitalised patients with COVID-19.

**Saturday, 6 June**
The Guardian reports that nearly 600 US health workers have died of COVID-19.

**Sunday, 7 June**
Three super-spreading events in an office, a restaurant and a bus show how easily SARS-CoV-2 can be spread over distances of more than 1 meter. The feature by *El País* is worth taking a look, even if you don’t understand Spanish: [https://elpais.com/ciencia/2020-06-06/radiografia-de-tres-brotes-asi-se-contagiaron-y-asi-podemos-evitarlo.html](https://elpais.com/ciencia/2020-06-06/radiografia-de-tres-brotes-asi-se-contagiaron-y-asi-podemos-evitarlo.html).

**Monday, 8 June**
Attending a sporting event, concert or play? Attending a wedding or a funeral? Stopping routinely wearing a face covering? Attending a church or other religious service? Hugging or shaking hands when greeting a friend? Going out with someone you don’t know well? When asked by The New York Times when they would expect to resume these activities of daily life, 42% to 64% of epidemiologists and infectious disease specialists answered they would prefer waiting a year before doing it again. The enquiry by Margot Sanger-Katz, Claire Cain Miller and Quoctrung Bui: *When 511 epidemiologists expect to fly, hug and do 18 other everyday activities again.*

It becomes increasingly clear that not all patients recover fully from SARS-CoV-2 infection. See ‘*It feels endless*: four women struggling to recover from Covid-19. (If you read Spanish, check also *Los últimos de la UCI*).
Dozens of new infections reported in Kabukicho, a district of more than 4,000 bars, restaurants and commercial sex establishments in Tokyo.

**Tuesday, 9 June**
New Zealand returns back to pre-COVID-19 life.
In Brazil, “poverty, poor access to health services and overcrowding all play a part in a disproportionate number of deaths”, reports The Guardian. Coronavirus death rates expose Brazil’s deep racial inequalities.

**Wednesday, V 10 June**
The Guardian publishes an analysis of the Surgisphere scandal (the retracted paper about hydroxychloroquine trial).
NIAID Director Anthony Fauci says the coronavirus pandemic is far from over.
The OECD says Britain will top the developing world’s recession league table.
British theatre might go out of business.

**Thursday, 11 June**
India, Mexico, Russia, Iran and Pakistan decide to end lockdowns.
Neil Ferguson, a former scientific adviser to the British government, says earlier restrictions could have halved the death toll.
If you read Spanish: Las mascarillas, claves para evitar una segunda oleada de la pandemia (El País).

**Friday, 12 June**
Beijing reimposes lockdown measures after a new COVID-19 outbreak around the wholesale market of Xinfadi (北京新发地水果批发市场).
Northwestern Memorial Hospital in Chicago announces that a young woman in her 20s whose lungs were destroyed by COVID-19 received a double lung transplant.
If you read French: Coronavirus – au cœur de la bataille immunitaire contre le virus.

**Saturday, 13 June**
What have Venice, Amsterdam and Barcelona in common? Before the COVID-19 pandemic they were overrun by tourists. Tourism certainly contributes to the wealth of these cities, but the vast majority of the populations – all those who are not directly or indirectly employed in mass tourism – receive no
benefits from millions of people transiting their neighborhood. The weekend of 13/14 June, just before the reopening of the Schengen area (see 15 June entry), is therefore a unique opportunity for people in hundreds of small and big charming cities throughout Europe. They enjoy the place where they live with those who were born there or chose to live there – like 10, 20 or 30 years ago, before the beginning of the tourist pandemic.

According to figures from the British Office for National Statistics (ONS), people living in more deprived areas are twice as likely to die from coronavirus (ONS | The Guardian).

Most Europeans now trust their leaders generally a little less than when the crisis began.

Malta’s abortion taboo leaves women in despair.

**Sunday, 14 June**

Lancet editor Richard Horton describes the management of the outbreak as ‘the greatest science policy failure of a generation’.

Immunologist Scott Canna and rheumatologist Rachel Tattersall publish a 23-minute audio about cytokine storms.

A study by Ben Etheridge and Lisa Spantig shows that one third of women suffered from lockdown loneliness.

Thailand, Malaysia, Vietnam... some countries managed to keep COVID at bay.

When should we send children back to school? Here is what 132 epidemiologists would be inclined to do.

**Monday, 15 June**

Mauro Giacca of King’s College London: “Covid-19 can result in complete disruption of the lung architecture.”

With a few exceptions, all borders in the European Schengen area are open again for free travel of European citizens. The Balearic Islands open to 11,000 German tourists.

Every stairway a marathon? There is no standard therapy for patients who have survived a severe corona infection. For many survivors, the way back to a normal life begins in rehabilitation clinics. If you read German, read this.

**Tuesday, 16 June**

Results from the RECOVERY trial: Dexamethasone is the first life-saving coronavirus drug (Study | The Guardian).
After hundreds of infections at the Xinfadi market, the Chinese authorities close all schools and call on residents to avoid “non-essential” travel outside of the city. Around thirty residential areas surrounding the market are quarantined. Companies are encouraged to favor teleworking and people can no longer, except in cases of force majeure, leave the capital. Around 67% of domestic flights are canceled. Libraries, museums, art galleries and parks can only operate at 30% of their capacity. Restaurants can no longer accommodate groups. Beijing begins screening tens of thousands of inhabitants, bringing its daily testing capacity to more than 90,000 people.

The U.S. Food and Drug Administration revokes its emergency use authorization for hydroxychloroquine sulfate and chloroquine phosphate to treat COVID-19.

Coronavirus cases rise in US prisons.

**Wednesday, 17 June**

Investigations from Nanjing show that turbulence from a toilet bowl can create a large plume that is potentially infectious to a bathroom’s next visitor ([Paper | The New York Times]).

After two women recently arrived from Britain were infected with COVID-19 and allowed to leave quarantine without being tested, New Zealand puts COVID-19 quarantine in the hands of the military.

**Thursday, 18 June**

The end of tourism? Christopher de Bellaigue publishes an insightful Guardian long read about the devastated global tourism industry. One key paragraph: “Tourism is an unusual industry in that the assets it monetizes – a view, a reef, a cathedral – do not belong to it. The world’s dominant cruise companies (…) pay little towards the upkeep of the public goods they live off. By incorporating themselves in overseas tax havens with benign environmental and labor laws – respectively Panama, Liberia and Bermuda – cruising’s big three, which account for three-quarters of the industry, get to enjoy low taxes and avoid much irksome regulation, while polluting the air and sea, eroding coastlines and pouring tens of millions of people into picturesque ports of call that often cannot cope with them.”

Eric Rubin and Lindsey Baden discuss SARS-CoV-2 transmission in a 20-minute audio by the New England Journal of Medicine.

A 13-day-old baby becomes one of the UK’s youngest victims.

Again, meat processing plants are proving to be ideal transmission settings. In the German town of Gütersloh, North Rhine-Westphalia, 657 employees test positive for SARS-CoV-2.

Richard Horton publishes The COVID-19 Catastrophe: What’s Gone Wrong and How to Stop It Happening Again. “The book returns again and again to the catastrophe in both the United Kingdom and the United States. It is haunted by the question: how did two of the richest, most powerful and most scientifically advanced countries in the world get it so wrong, and cause such ongoing pain for their citizens?” (Nature)

Friday, 19 June

Beijing residents react with frustration and anxiety after finding almost 200 new cases of coronavirus.

A study by the Italian Istituto Superiore di Sanità detects SARS-CoV-2 RNA in wastewater samples collected in Milan and Turin on 18 December 2019.

Investigations from the University of Sussex describe society as regressing back to the 1950s for many women (The Guardian).

UK abandons developing its own contact-tracing app and switches to the alternative design by Google and Apple.

Three experts exchange their views on the risks of travelling by plane.

Alexandra Villarreal describes a new American way of life: some Americans return to bars, dining and beaches, others shy away, concerned that the virus is still raging.

Sunday, 20 June

Spain plunges into the so-called new normal after 98 days of COVID-19 state-of-alarm.

The coronavirus outbreak in the German meat processing plant Tönnies near Gütersloh continues. By midday, 1,029 employees test positive and 2,098 negative for SARS-CoV-2. Nineteen people, almost all employees of Tönnies, are being treated for COVID-19. Six of them are in intensive care, two patients are ventilated (DIE ZEIT).

Those who might be tempted to attend a political rally should read the summary of COVID Reference’s Transmission chapter:
1. It appears that a high percentage (as high as 80%?) of secondary transmissions could be caused by a small fraction of infectious individuals (as low as 10%?; Endo 2020); if this is the case, then the more people are grouped together, the higher the probability that a superspreader is part of the group.

2. It also appears that aerosol transmission might play an important role in SARS-CoV-2 transmission (Prather 2020); if this is the case, then building a wall around this same group of people and putting a ceiling above them further enhances the probability of SARS-CoV-2 infection.

3. It finally appears that shouting and speaking loudly emits thousands of oral fluid droplets per second which could linger in the air for minutes (Anfinrud 2020, Stadnytskyi 2020, Chao 2020, Asadi 2019); if this is the case, then creating noise (machines, music) around people grouped in a closed environment would create the perfect setting for a superspreader event.

Stay away from mass gatherings.

**Week 26**

This week has seen important local outbreaks. The recurring patterns: family celebrations (Melbourne, Berlin, Lagos) and people living (Malaga, Lisbon), working (Gütersloh, Tokyo, Huesca) or playing (Adria Tennis Tour) close together. The next outbreaks are anticipated in Liverpool, Naples (football celebrations) and some Italian cities (movida).

On 24 June, the US established a new national SARS-CoV-2 record. In Texas, the number of deaths is expected to increase about two to three weeks from now.

**Sunday, 21 June**

The number of infections in the Gütersloh (Germany) meat-processing plant exceeds one thousand. Nearly 7,000 employees are quarantined. After repeated outbreaks in the meat industry, The Guardian publishes *Why you should go animal-free: 18 arguments for eating meat debunked.*

The Spanish authorities increase the purchase of flu vaccines. Immunizations will start as soon as possible and priority will be given to health personnel.

**Monday, 22 June**

France reopens schools, colleges, kindergartens, cinemas, game rooms and small sports.
In India, 25 luxury hotels are to be transformed into COVID-19 care centers. Injectable dexamethasone is more difficult to manufacture than tablets, and could soon run out.

The New York Times publishes *Lessons on Coronavirus Testing From the Adult Film Industry*.

**Wednesday, 24 June**

More than 1,500 workers have tested positive in Gütersloh, Germany. The abattoir cooling systems may have contributed to spreading aerosol droplets laden with coronavirus. The authorities order a lockdown for 640,000 people.

In the US, more than 38,000 cases are detected, a record since the start of the coronavirus epidemic. The states that lifted containment measures, mainly governed by Republicans, are the most affected.

Daily New Cases in Texas

![Daily New Cases](source: https://www.worldometers.info/coronavirus/usa/texas)

Income emerges as a major predictor of coronavirus infections, along with race.

Tennis player Novak Djokovic tests positive for COVID-19 amid Adria Tour fiasco (dixit Le Monde: Adria Cluster Tour).

The Guardian publishes *The coronavirus backlash: how the pandemic is destroying women's rights*.
**Thursday, 25 June**

In young children, SARS-CoV-2 infection is largely asymptomatic or accompanied by few symptoms. Now, two pre-published studies by Fontanet et al. from the Institut Pasteur, Paris, also suggest lower infection rates in a French primary school (6 to 11-years-old) when compared to a high school in Crépy-en-Valois, a small town 60 km northeast of Paris. The studies show that 38% of high school students had antibodies against SARS-CoV-2, but only 8.8% of primary school students in the same town (see following table).

A study of residents in the Alpine ski resort of Ischgl find that 42% have antibodies for the virus.

More than 80 people test positive in an outbreak at a Red Cross center in Malaga.

Tokyo detects new outbreaks of coronavirus in offices, with 55 new cases, its biggest rebound in a month and a half.

<table>
<thead>
<tr>
<th></th>
<th>High school students*</th>
<th>Children in primary school**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pupils</td>
<td>240</td>
<td>510</td>
</tr>
<tr>
<td>Parents</td>
<td>211</td>
<td>641</td>
</tr>
<tr>
<td>Close family</td>
<td>127</td>
<td>119</td>
</tr>
<tr>
<td>Teachers</td>
<td>53</td>
<td>42</td>
</tr>
<tr>
<td>Staff</td>
<td>27</td>
<td>28</td>
</tr>
<tr>
<td>Others</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>661</td>
<td>1 340</td>
</tr>
</tbody>
</table>

** Press report (Le Monde), incomplete data
*** Siblings

Sokolowska et al. publish *Immunology of COVID-19: Mechanisms, Clinical Outcome, Diagnostics and Perspectives - A Report of the European Academy of Allergy and Clinical Immunology (EAACI)*

The Guardian publishes *On different planets: how Germany tackled the pandemic, and Britain flailed.*

The New York Times publishes *How the Virus Won*, analyzing travel patterns, hidden infections and genetic data to show how the epidemic spun out of control.

Liverpool wins Premier League. At the title party, thousands gather on the streets without face masks. Rallies on UK beaches and at street parties in London.
Friday, 26 June


The Guardian publishes *I’m a viral immunologist. Here's what antibody tests for Covid-19 tell us.*

The New York Time publishes *How the Coronavirus Short-Circuits the Immune System* and *Can Covid Damage the Brain?*

Saturday, 27 June

The European Union is preparing to restrict most US residents from visiting the region.

If you read Spanish, read *Más de 100 días arrastrando el coronavirus* by Isabel Valdés.

If you read French, read *Qu’est-ce que le « R0 », le taux de reproduction du virus ?* by Gary Dagorn.

If you read Portuguese, read *Durante a Gripe Espanhola, houve uma Liga Anti-Máscara. E tudo piorou.*

Week 27

This week witnesses an important resurgence of SARS-CoV-2 infections in the US and India. Meanwhile, Europe which has more or less successfully managed the first wave, is holding its breath: will the economically all-important tourist season smoothly go ahead or will it be grounded by a second COVID wave? For now, smaller outbreaks (Gütersloh, Leicester, Lleida) are being kept under control. In this context, the opening of closed space where strangers can meet (bars, brothels and restaurants) may not be a good idea.

In the meantime, the EU opens its borders to 15 countries, car rental companies expect to lose up to 80%, Gilead imposes a price of about 350 euros per dose for its (weak) anti-SARS-CoV-2 drug, China starts testing a vaccine on military personnel, and asymptomatic spread continues – why shouldn’t it.

Astonishingly, the question of using face masks continues to be debated. While you can probably do without them in low-prevalence areas such as most parts of Southern Italy, you are well- ADVISED to wear them in the US. A British journalist stated that not wearing face masks in epidemiological hotspots is like driving drunk. Imagine how people feel who are governed by drunkards.
**Sunday, 28 June**

Ten million official cases and 500,000 COVID-19 deaths.

Source: Johns Hopkins Coronavirus Resource Center.

**Monday, 29 June**

Chinese CanSino Biologics receives the green light to use a recombinant novel coronavirus vaccine (Ad5-nCoV) within the military.

**Tuesday, 30 June**

Anthony Fauci warns that a “general anti-science, anti-authority, anti-vaccine feeling” is likely to thwart vaccination efforts (The Guardian).

India has more than 450,000 confirmed cases, making it the world’s fourth-worst-hit country. Major cities such as Delhi and Mumbai are particularly badly affected (Nature).

China cuts off more than 400,000 people in Anxin county to tackle a small COVID-19 cluster (The Guardian).

The new poor in Italy? Only a small percentage of companies have received promised lockdown help (The Guardian).

The English city of Leicester is in local confinement again after 866 new cases are diagnosed in two weeks.

The pharmaceutical company Gilead imposes a price of about 350 euros per dose for its (weak) anti-SARS-CoV-2 drug.

The New England Journal and The Lancet publish three articles (one | two | three) and a comment about Multisystem Inflammatory Syndrome in Children (MIS-C).
July

Wednesday, 1 July
The New York Times publishes an update on super-spreaders. Outbreak in Melbourne, Australia. The authorities confine 300,000 people in 30 neighborhoods for a month. The EU publishes a list of 15 countries from where people should be allowed into the Union. Visitors from the US to remain banned from entering the EU because of the country’s rising infection rate. The US buys up the world stock of remdesivir. We discover this YouTube video by Tang and al. visualizing airflow patterns associated with common, everyday respiratory activities. In this case, talking illustrates rapidly changing airflow patterns exchanged between talkers. Testing finds cases at US meat-processing plants but officials refuse to release the information (The Guardian). According to an article by Science, only 50% of Americans plan to get a COVID-19 vaccine.

Thursday, 2 July
California rolls back the reopening of bars, restaurants and indoor venues (The Guardian). Anthony S. Fauci and H. Clifford Lane publish Four Decades of HIV/AIDS — Much Accomplished, Much to Do. Nicholas Kristof publishes Refusing to Wear a Mask Is Like Driving Drunk.

Friday, 3 July
Cheng et al. publish How to Safely Reopen Colleges and Universities During COVID-19: Experiences From Taiwan. The Guardian describes the new emergency in Los Angeles.

Saturday, 4 July
The HIV drug lopinavir/ritonavir fails to reduce mortality in an interim analysis of the Solidarity trial. WHO discontinues both the lopinavir/ritonavir and the hydroxychloroquine treatment arms for COVID-19 (who.int).
After SARS-CoV-2 outbreaks in fruit companies, a nursing home, a neighborhood community and a hostel for homeless people, Catalonia imposes a lockdown on 200,000 people around Lleida.

The epidemic is taking off in the US:

![Daily New Cases](https://www.worldometers.info/coronavirus/country/us/)

Source: [https://www.worldometers.info/coronavirus/country/us/](https://www.worldometers.info/coronavirus/country/us/)

Adam Gabbatt publishes *Fourth of July celebrations increase risk of 'superspreader' events.*

Jesse Wegman publishes *Seriously, Just Wear Your Mask.*

Michelle Cottle publishes *Florida, America’s Pandemic Playground.*

Pubs reopen in England.

**Week 28**

Week 28 will be recorded as a watershed in the perception of SARS-CoV-2 transmission risk: yes, the virus is transmitted by fat droplets, and yes, it is also transmitted tiny aerosol particles. If this shift is proven to be right, SARS-CoV-2 may go down in history as the virus that unified the almost century-old dichotomy of droplets vs. aerosol transmission. The merit goes to Lidia Morawska and Donald K. Milton, supported by 237 scientists (see also the comment in *The Guardian* and in *The New York Times*). In the next days, we will publish an update of our Transmission chapter.

Paterson et al. publish a worrisome article about the neurological complications of COVID-19.

Second waves are leading to partial lockdowns in Australia, Spain, Serbia and Israel while Catalonia and the Balearic Islands order wearing face masks even when the required 1.5-metre social distancing can be observed.
The first wave continues in the US. People in Mexico border towns try to stop Americans from crossing.

**Sunday, 5 July**


Spain puts part of Galicia back into lockdown.

**Monday, 6 July**

Find out how Anthony Fauci, Elizabeth Connick, Paul A. Volberding, Linda Bell, Barry Bloom and David Satcher deal with COVID-19 risks in their everyday lives.

**Tuesday, 7 July**

If you read Spanish, read “La enigmática mutación del coronavirus que ahora domina el planeta” (El País).

**Wednesday, 8 July**

COVID-19 fears: People in Mexico border towns try to stop Americans from crossing (The Guardian).

Paterson et al. publish *The emerging spectrum of COVID-19 neurology: clinical, radiological and laboratory findings*. See also the article published in The Guardian.

Violence at Belgrade protest over renewed lockdown measures

Churches at risk: SARS-CoV-2 infiltrates Sunday services, church meetings and youth camps. More than 650 cases have been linked to reopened religious facilities.

Second COVID-19 wave in Israel.

**Thursday, 9 July**

WHO update information about SARS-CoV-2 transmission (*WHO 20200709*): “There have been reported outbreaks of COVID-19 in some closed settings, such as restaurants, nightclubs, places of worship or places of work where people may be shouting, talking, or singing. In these outbreaks, aerosol transmission, particularly in these indoor locations where there are crowded...
and inadequately ventilated spaces where infected persons spend long periods of time with others, cannot be ruled out.”

Five million Melbourne residents are locked down again (read also this article).

Catalonia orders wearing face masks even when the required 1.5-metre social distancing can be observed. The fine for not observing the new rules: 100 euros. The Balearic islands is set to follow Catalonia’s lead soon.

The Tokyo authorities pay nightclubs as well as host and hostess bars thousands of dollars if they close for more than 10 days.

Indonesia announces a new cluster of more than 1,000 cases at a military training center in West Java.

**Friday, 10 July**

Guardian live (10 July): Bogotá to re-enter strict lockdown.

The Guardian Global report (10 July).

Rats torment New York alfresco diners.

Scotland asserts separateness from England.

If you read Spanish, read El mapa de los brotes de coronavirus: el 40% tiene su origen en encuentros familiares.

**Saturday, 11 July**

The Guardian: Coronavirus live + Global report.

New outbreak in Spain in L’Hospitalet, the second biggest city in the Barcelona metropolitan area (3.2 million people; El País).

Over 40 Florida hospitals max out their intensive care unit capacity (The Guardian).

Rapid serological tests are now available in French pharmacies. The test requires taking a drop of blood by pricking the skin, usually at the fingertip, then putting it in contact with a reagent. The result appears in a few minutes (Le Monde).

The NY Times publishes ‘I Couldn’t Do Anything’: The Virus and an E.R. Doctor’s Suicide.

If you read Spanish, read the Fauci interview “La cuestión es que todo el mundo debería llevar mascarilla” (El País).

Is the governor of the hard-hit Lombardy region (almost 50% of all Italian cases) opening the dance for the second wave in his country? In a bold (suicidal?) move he allows discos to reopen open-air discos. The Repubblica
newspaper reports that people “filled the slopes of the main Milanese discos without wearing personal protective equipment and without respecting the social distancing.” The countdown has begun.

**Week 29**

This week, the publication of detailed results of a phase 1, dose-escalation, open-label trial (14 July) reminded us that the race for a vaccine is gaining momentum. More encouraging results from competitor researchers are expected within days.

Meanwhile, the pandemic is gaining momentum, too, with sad records recorded from all over the world. A new area of concern is Europe, where a second wave may be building up (18 July). In contrast to what happened in March, local epidemics seem now to be fueled by the infection of younger people. Wearing face masks may soon be required in many European countries (16 July).

In the US, daily new SARS-CoV-2 cases are on track to go beyond 100,000. As Rudolf Virchow, the great 19th century father of pathological anatomy, liked to say: “An epidemic is a social phenomenon that has some medical aspects.” (Cited by Bernard Henri-Lévy in *Ce virus qui rend fou*, Grasset, June 2020)

**Sunday, 12 July**

Fourteen renowned doctors (Antoine Pelissolo, Jimmy Mohamed Philippe Amouyel, Francis Berenbaum, Eric Caumes, Robert Cohen, Anne-Claude Crémieux, Gilbert Deray, Vianney Descroix, Philippe Juvin, Axel Kahn, Karine Lacombe, Bruno Megarbane and Christine Rouzioux) demand “the wearing of a mandatory mask in all enclosed public places” in order to prevent a second COVID-19 wave (Le Parisien, Le Monde).

In Sydney, thousands of pub-goers have been asked to self-isolate for two weeks after a hotel staff member and three other people became the latest cases in an emerging coronavirus cluster (The Guardian).


If you read Spanish, read *Los delirios mortales del rey Donald*, by Paul Krugman, and *Jornaleros de la pandemia*, by Guillermo Abril.
Monday, 13 July

California, 40 million people, return to the closure of all indoor operations for restaurants, wineries, movie theaters and family entertainment, zoos, museums and cardrooms bars. The state is one of the main SARS-CoV-2 foci in the United States (more than 300,000 cases, 7,000 deaths).

A study examining data for 355 Dutch municipalities finds evidence of a positive relationship between air pollution and Covid-19 cases, hospital admissions and deaths (Cole MA, Ozgen C, Strobl E (PDF); The Guardian).

The Guardian: 30-year-old dies after attending ’Covid party’ in Texas | ‘I think I made a mistake, I thought this was a hoax, but it’s not.’ See also the video by Jane Appleby.

Do men without a mask look tough? (The Guardian)

Returning German tourists as superspreaders? The CEO of the World Medical Association Frank Ulrich Montgomery proposes a two-week quarantine for holidaymakers returning from the Mallorca island (audio in German) after hundreds of drunken tourists celebrate in a pre-COVID atmosphere.

No re-opening of discos in France as the French Council of State estimates that the prolonged closing of the night clubs is not “disproportionate” (Le Monde).

Tuesday, 14 July

Jackson et al. publish a preliminary report about 45 healthy adults, 18 to 55 years of age, who received two vaccinations, 28 days apart, with mRNA-1273 in a dose of 25 μg, 100 μg, or 250 μg. Read also the editorial by Editorial by Penny M. Heaton: The Covid-19 Vaccine Development Multiverse and the audio interview Covid-19 Vaccine Development, by Rubin, Baden and Morrissey.

Israel, Uzbekistan, Melbourne, California – certain states, areas and cities enter new lockdowns. Le Monde updates a non-exhaustive list of new pandemic hotspots, classified by number of inhabitants concerned and by country.


Twitter comment on British tourists in Spain: “Parts of Spain in lockdown, the elderly shut away in care homes, we all wear masks in the street, but in Magaluf the antisocial and irresponsible Brits do whatever they please. It’s shameful.” (The Guardian, text and video)
**Wednesday, 15 July**

If you read Spanish, read *Una sanitaria en L'Hospitalet de Llobregat: “El ambulatorio roza el colapso, peor que en abril”*. *(El País)*.


**Thursday, 16 July**

The French government decides that wearing mask will be compulsory in closed public places from next week. They describe the situation as “problematic” in Mayenne, “worrying” in New Aquitaine, and increasing number of cases in Paris and in Finistère. *(Le Monde)*

In Spain, 40% of recent outbreaks might have been associated with family events (“...a wedding in Tudela, a celebration of San Juan in a neighborhood of Castellón, a meal with friends in Alcanar (Tarragona).” *(El País)*.

In a response to the paper by Jackson et al. (see 14 July), British researchers working on another Covid-19 vaccine at the University of Oxford spread the word that their vaccine, too, triggers two types of immune response: the production of antibodies – proteins that can bind to the virus, preventing it from entering cells and flagging it to immune cells – but it also seems to result in the production of “killer” T cells – immune cells that attack infected human cells. *(The Guardian)*

Danielle Renwick publishes *How quickly will there be a vaccine? And what if people refuse to get it?* *(The Guardian)*


If you read Spanish, read Miguel Ángel Criado: *Más de la mitad de los españoles ingresados por coronavirus han desarrollado problemas neurológicos* *(El País)*

**Friday, 17 July**

Israel returns to partial lockdown. All indoor gatherings of 10 or more people are banned. Restaurants return to takeaways and deliveries only. During the weekend, all shops, hairdressers and attractions are closed. All gyms and fitness studios are closed at all times.
Saturday, 18 July

Spain seems on the brink of a second COVID-19 wave. In the last 7 days, the country had 10 times more new cases than a month ago (El País). Four million residents of Barcelona and 12 municipalities around the city have been urged to stay at home. The regional Government announces that the restrictions also include the reduction of capacity in bars and restaurants and closure of nightlife venues, cultural activities and gyms, and a ban on gatherings of more than 10 people from Saturday.

In France, which already announced plans to make mask wearing mandatory in enclosed public spaces, authorities reported a sharp rise in the infection rate in Brittany. According to data released on Friday, the disease's reproduction rate in Brittany has risen from 0.92 to 2.62 between 10-14 July.

Infections in India pass one million.


Week 30

This week may be recalled as the timid beginning of the second European COVID-19 wave. At the beginning of the week, bars in Barcelona were ordered to limit the number of clients. On Saturday, Norway and the UK imposed a 10 (UK: 14) day quarantine on all people coming back from Spain, mostly holidaymakers, and Barcelona ordered the closure of discos, dance halls, etc. All over the continent, outbreaks are linked to seasonal farm laborers, family meetings and nightlife. 2020 tourism was severely affected by the continent-wide spring lockdowns. It is now doubtful that the holiday season will continue to summer’s end.

The daily new cases in Australia:
Monday, 20 July

This is vaccine day. Andrew Pollard and colleagues report their phase 1/2 randomized trial of a chimpanzee adenovirus-vectorized vaccine (ChAdOx1 nCoV-19); and Wei Chen and colleagues report results from a randomized phase 2 trial of an Ad5-vectorized COVID-19 vaccine. Read also the comment by Naor Bar-Zeev and William John Moss.

In Sao Paulo, 900 health professionals will participate in a phase 3 trial of a vaccine developed by the Chinese Sinovac Biotech laboratory. In total, the vaccine will be offered to 9,000 volunteers in six Brazilian states.

In France, the wearing of a mask becomes compulsory in closed places which are open to the public.

In Barcelona, the capacity in bars is limited to 50%. Visits to nursing homes are prohibited.

Tuesday, 21 July

Historic pact of the European Union to overcome the COVID-19 crisis: for the first time in its history, the EU member states will borrow money to finance an extraordinary economic stimulus with 390,000 million in grants and 360,000 million in credits, sending a strong message that they will continue to stay together. Presidents in the east and in the west will have taken notice (see also The Guardian).

Indian authorities claim that SARS-CoV-2 antibody testing of people living in the Delhi region showed that 23.5% had antibodies against the virus. Samples
from 21,387 people were examined. This percentage would be 50 times higher than the officially reported figures. Delhi, with a population of 29 million, has reported only 123,747 infections.

Jennifer Steinhauer and Thomas Gibbons-Neff explain how American military officials are trying to contain the spread of the SARS-Cov-2 in its ranks (The New York Times).

See also the feature by The Guardian: How coronavirus is reshaping Europe's tourism hotspots. An opportunity to rethink their business model? Barcelona reduces the capacity of its beaches (El País).

**Wednesday, 22 July**

Belgium is recording a significant increase in Covid-19 cases. During the period July 12-18, the number of new infections rose 89% with an average of 184 cases diagnosed per day, up from 98 the week before. Most cases are among people between 20 and 59 years old who were infected during parties or gatherings.

On the eve of a four-day long weekend in Japan, the governor of Tokyo calls on her constituents to stay at home, as the number of new daily cases of Covid-19 is sharply increasing in the region. As Covid-19 infections appear to be spreading widely, the Japanese capital is on its maximum alert level.

In Spain, 40% of people newly infected with SARS-CoV-2 are under 40 years of age and most do not know where they have been infected.

**Thursday, 23 July**

The Spanish newspaper El País sounds the alarm: The virus rebounds in Spain: data from 10 communities show more infections and more hospitalizations.

In the U.S., SARS-CoV2 testing laboratories struggle to find the chemicals and plastic pieces they need to carry out coronavirus tests (The New York Times). Lazaro Gamio, Sarah Mervosh and Keith Collins show Where the Virus Is Sending People to Hospitals.

**Friday, 24 July**

Authorities order the closure of nightlife (discos, dance halls, etc.) in Catalonia for at least 15 days. The hours of activity in casinos and game rooms are limited until midnight (El País + El País).

Norway reinstates mandatory 10-day quarantine for travelers coming back from Spain.
The U.K. makes wearing masks compulsory in stores.
The New York Times and El País ask “Who will receive the first COVID vaccines?”
Lauren Leatherby publishes How the U.S. compares With the world’s worst coronavirus hot spots.

Saturday, 25 July
Catalonia exceeds 50 hospitalized daily, 10 times more than the figures reported by the Ministry of Health (El País).
In Belgium, wearing masks is now compulsory on markets, in shopping streets, in hotels, cafes and restaurants (except at the table).
With immediate effect, the UK re-quarantines travelers from Spain. Those who come back home must isolate themselves for 14 days. This measure will affect Spain’s tourism industry. But not only Spain is suffering.
If you read Spanish, read El coronavirus ha repuntado en 30 provincias: el mapa con la situación de los contagios en cada una | En el último mes han aumentado los casos y las hospitalizaciones en media España (El País).

Sunday, 26 July
A surge in COVID-19 cases has forced a hospital in rural Texas to set up “death panels” to decide which patients it can save and which ones will be sent home to die. By Michael Sainato.
Victoria, Australia, reports a national record of 10 Covid-19 deaths.
North Korea reports the first COVID-19 case (...) and declares a state of emergency (The Guardian).
How Hawaii avoided a coronavirus spike, but severely damaged its economy. Lauren Aratani explains.
If you read Spanish, read this: Un verano con virus: qué hacer | Viajar con amigos o ir a visitar a la familia unos días entraña riesgos. ¿Se comparte el salón? ¿Y el coche? ¿Se puede ligar? Los expertos explican cómo minimizar la exposición.
The true number of excess deaths due to COVID-19 is probably more than 50% higher than the officially reported data. See the analysis by El País.
Monday, 27 July

If you understand German, meet Dr Camilla Rothe (6 minutes) who tested the detected the first SARS-CoV-2 positive patient in Germany at the end of January. Within days, it became clear that asymptomatic transmission would play an important role in the pandemic. In the video interview, Dr Rothe looks back - and forward.
Notes
Second waves, third waves, never ending waves — as the world is about to enter the second year of the SARS-CoV-2 pandemic, people realize that they are just at the beginning of a global health and economic crisis. In the Northern Hemisphere, the 6 dark autumn and winter months have begun and the world is holding its breath: will the new coronavirus follow the track of the 1918 flu epidemic, relatively mild in spring and devastating in autumn and winter?

There is no doubt that the immense resources of medicine and biotechnology will soon produce a safe and effective vaccine; however, only fools expect mass vaccinations before the middle of 2021 and a measurable impact on the pandemic before 2022.

In the meantime, people around the globe will reduce their contacts with other people and perfect their skills of social distancing. They will continue to wear face masks next year, the year after and maybe beyond. It isn’t fun but it must be done.