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Review

Potential sources, modes of transmission and effectiveness of prevention measures against SARS-CoV-2

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SUMMARY

During the current SARS-CoV-2 pandemic new studies are emerging daily providing novel information about sources, transmission risks and possible prevention measures. In this review, we aimed to comprehensively summarize the current evidence on possible sources for SARS-CoV-2, including evaluation of transmission risks and effectiveness of applied prevention measures. Next to symptomatic patients, asymptomatic or pre-symptomatic carriers are a possible source with respiratory secretions as the most likely cause for viral transmission. Air and inanimate surfaces may be sources; however, viral RNA has been inconsistently detected. Similarly, even though SARS-CoV-2 RNA has been detected on or in personal protective equipment (PPE), blood, urine, eyes, the gastrointestinal tract and pets, these sources are currently thought to play a negligible role for transmission. Finally, various prevention measures such as handwashing, hand disinfection, face masks, gloves, surface disinfection or physical distancing for the healthcare setting and in public are analysed for their expected protective effect.

Introduction

The cumulative number of COVID-19 cases continues to increase rapidly through different countries around the world [1], however the exact source of transmission in new cases frequently remains unknown. Therefore, a variety of emergency responses and policy strategies mainly based on physical distancing measures with the aim to reduce close contact between people in public and healthcare facilities have been implemented in most countries [2]. In addition, a broad range of individual measurements such as plastic shields at cash registers, homemade face masks, wearing plastic gloves, disinfection of frequently touched surfaces can be seen in the public, indicating a great uncertainty how SARS-CoV-2 can and cannot be transmitted. In this review we summarized the

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current knowledge regarding potential sources of SARS-CoV-2 infection including the role of asymptomatic cases and body fluids and evaluated the potential capacity of different precautions to prevent transmission of SARS-CoV-2.

Search strategy and selection criteria

References for this review were identified through searches of PubMed for articles published until 26 June 2020. The following terms were used in combination with SARS-CoV-2: air (283 hits), viral load (182 hits), tear (43 hits), conjunctiva (26 hits), surface (292 hits), environmental (855 hits), pets (15 hits) and personal protective equipment (538 hits). In combination with COVID the following terms were used: viral load (199 hits), asymptomatic (776 hits), pets (15 hits) and cluster (492 hits). Additional relevant articles were identified in the authors' personal files. Articles were selected and data extracted when they provided evidence on viral carriage (symptomatic, asymptomatic and pre-symptomatic), viral load in body secretions and fluids, modes of transmission and contamination rates of objects.

Infectious dose

Humans can acquire devastating infectious diseases through exposure to very low levels of infectious particles. For example, only a few cells of *Mycobacterium tuberculosis* are required to overcome normal lung clearance and inactivation mechanisms in a susceptible host [3]. While the infectious dose for SARS-CoV-2 is currently still unknown, cell culture and animal experiments are warranted to provide more insights into the infectivity and infectious dose of SARS-CoV-2.

Relevance to determine viral infectivity

It is noteworthy that the presence of viral RNA in specimens does not always correlate with viral transmissibility and infectivity [4]. Hence, it was questioned early on whether SARS-CoV-2 viral RNA load correlates with culturable virus [5]. One study showed that SARS-CoV-2 was detected by culture in 19 of 25 clinical samples (nasopharyngeal swab) from COVID-19 patients [6]. Another study showed that infectious virus isolated by culture was only detected during the first week of symptoms (16.7% of swab samples; 83.3% in sputum samples); no isolates were obtained from samples taken after day 8 in spite of ongoing high viral RNA loads [7]. In contrast, a significant correlation between Ct value and culture positivity rate was observed in nasopharyngeal samples [8]. In a ferret model of H1N1 infection, the loss of viral culture positivity but not the absence of viral RNA coincided with the end of the infectious period. In fact, real-time reverse transcriptase polymerase chain reaction (PCR) results remained positive 6—8 days after the loss of transmissibility [9]. For SARS coronavirus, viral RNA was detectable in the respiratory secretions and stools of some patients after onset of illness for more than 1 month, but live virus could not be detected by culture after week 3 [10]. The inability to differentiate between infective and non-infective (dead or antibody-neutralized) viruses therefore remains a major limitation of nucleic acid detection methods. Despite this limitation, given the difficulties in culturing infectious virus from clinical specimens during a pandemic, using viral RNA load as a surrogate remains plausible for generating careful clinical hypotheses.

Association of viral load with symptoms and outcome

The association between viral load and clinical outcome including severity of symptoms is still poorly characterized although the majority of studies reported an association between higher viral loads and more severe symptoms [11—19].

Transmission dynamics

Transmission dynamics of SARS-CoV-2 are heterogeneous [20]. Numerous individual infection clusters in particular in Asia with variable size have been reported [21—31]. Originating from a single travel-associated primary case from China, the first documented chain of multiple human-to-human transmissions of SARS-CoV-2 outside of Asia allowed a detailed study of transmission events and identified several factors (e.g., cumulative face-to-face contact, direct contact with secretions or body fluids of a patient, PPE) to classify contacts as low or high risk [32]. Furthermore, factors such as immune suppression, increased disease severity and viral load, asymptomatic individuals, the practice of seeking care at multiple healthcare facilities, frequent inter-hospital transfer, large numbers of contacts and prolonged duration of exposure facilitate transmission [33]. Household transmission is also common [34]. Superspreading is regarded as a normal feature of disease spread and has also been described with SARS-CoV-2 [35,36]. Importantly, a recent study observed that transmission clusters occurred in many, predominantly indoor settings and most clusters involved fewer than 100 cases, with the exceptions being in healthcare (hospitals and elderly care), large religious gatherings, food-processing plants, schools, shopping centres, and large co-habiting settings (worker dormitories, prisons and ships) [31]. Given the predominately mild, non-specific symptoms, infectiousness before symptom onset the successful containment of COVID-19 relies on stringent and urgent surveillance and infection-control measures.

Epidemiological relevance of asymptomatic SARS-CoV-2 cases

Based on the definition of the WHO a confirmed case is a person with laboratory confirmation (detection of viral genomic material) of SARS-CoV-2, irrespective of clinical signs and symptoms [37]. Asymptomatic coronavirus infections have been described before [38] and might together with pre-symptomatic spread form a potential source of COVID-19 infections acquired in a social or nosocomial context [26,39—44]. In February 2020, a total of 44,672 confirmed cases were reported for China with a proportion of 1.2% of asymptomatic cases [45]. Data from the first of April 2020 based on more rigorous testing of contact persons suggest in a small cohort of 166 new cases a proportion of 78% as asymptomatic cases [46]. Irrespective of the frequency of asymptomatic carriers, they are considered to be important for the transmission of the disease [47]. Various studies reported SARS-CoV-2 infections, originating from asymptomatic carriers during close contacts such as household contacts or residents of a long-term-care skilled nursing facility [43,48–52]. Importantly, several studies have reported that viral RNA loads in pre-symptomatic, asymptomatic and symptomatic patients do not differ significantly [53–55]. Others have reported no transmission from 455 contacts (patients, family members, hospital staff) to asymptomatic carriers and concluded that the infectivity of some asymptomatic carriers may be weak [56].

As summarized in Table I, the proportions of asymptomatic SARS-CoV-2 cases at the time point of testing have been determined for different cohorts of patients. In hospitalized patients it was described to range between 5.0% and 27.8% [57–60]. In a long-term care facility, it was quite high at 56.5% [61]. In family clusters it was found to be between 25% and 57.1% [62,63]. In 171 children in China, the proportion was 15.5% [64]. Among Japanese nationals evacuated from Wuhan by chartered flights it was 30.8% in contrast to German nationals with 1.8% [65,66]. On board a cruise ship, asymptomatic carriers were detected in 50.5% of the cases. The delay-adjusted asymptomatic proportion, however, was only 17.9% [67]. In Iceland, a proportion of 3.6% of the general population (13,080 of 364,000 inhabitants) were investigated. Overall, 100 of them (0.8%) were positive with a proportion of 43% asymptomatic carriers. Among inhabitants with a high risk for infection the proportion of asymptomatic cases was only 7% [68]. Overall, asymptomatic SARS-CoV-2 infections seem to account for up to 56% of SARS-CoV-2 infections in selected cohorts, suggesting that it is a significant factor for the rapid progression of the COVID-19 pandemic [53,69,70].

For comparison, the prevalence of asymptomatic influenza virus carriage (total absence of symptoms) ranged from 5.2% to 35.5% and subclinical cases (illness that did not meet the criteria for acute respiratory or influenza-like illness) between 25.4% and 61.8% [71]. With MERS, a proportion of 9.5% of 1010 cases was asymptomatic [38].

Follow-up examinations, however, indicate that the majority of initially tested asymptomatic cases (70.8–100%) develop moderate but detectable clinical symptoms over time and therefore should be considered pre-symptomatic. Only in a small group of patients did no symptoms or radiological findings became apparent, but they were described as potentially infectious for up to 29 days (Table II) [72].

Of note, patients with negative PCR results prior to discharge may also become transient asymptomatic carriers again. One patient, for example, was retested positive for SARS-CoV-2 during the 2 weeks of quarantine after discharge [73]. Two healthcare workers (HCWs) were also tested (throat swab) after discharge (COVID-19) and were weakly positive in two of seven samples and positive in one of seven samples (case 1 sampled over 10 days), and weakly positive in one of eight samples and positive in one of eight samples (case 2 sampled over 8 days) [74]. However, these results have to be interpreted with caution as currently applied PCR methods can lead to fluctuating results in weakly positive samples due to detection limits of the assays. Indeed, a single case was described with low viral RNA loads or negative RT-qPCR results, despite a SARS-CoV-2 infection confirmed by the presence of anti-SARS-CoV-2 specific antibodies [75]. Importantly, a

Table I
Proportion of asymptomatic carriers in selected COVID-19 cohorts

Type of cohort	Size of cohort	Number of tested individuals	Number of positive tests ('cases')	Proportion of asymptomatic cases at the time of testing (*N*)	Reference
Hospitalized COVID-19 patients in Peking	262	262	262	5.0% (13)	[57]
First 28 cases in South Korea	28	28	28	10.7% (3)	[58]
Hospitalized COVID-19 patients in Wuhan	81	81	81	18.5% (15)	[59]
Hospitalized COVID-19 children in Zhejiang	36	36	36	27.8% (10)	[60]
Long-term care facility	82	76	23	56.5% (13)	[61]
Family cluster	9	9	8	25% (2)	[62]
Family aggregation	7	7	7	57.1% (4)	[63]
Japanese nationals evacuated from Wuhan by chartered flights	565	565	13	30.8% (4)	[65]
German nationals evacuated from Wuhan by chartered flights	126	114	2	100% (2)	[66]
Passengers and crew members on board a cruise ship	3711	3063	634	50.5% (320)	[67]
Children with known contact with persons having confirmed or suspected SARS-CoV-2 infection	1391	1391	171	15.5% (27)	[64]
Iceland inhabitants with a high risk for infection	9199	9199	1221	7%*	[68]
Iceland general population	364000	13080	100	43%*	[68]
Children from family clusters	74	74	74	29.7% (22)	[194]
Nursing facility	89	76	48	56% (27)	[53]
Healthy passengers from cruise ship	215	215	9	67% (6)	[195]
Asymptomatic healthcare workers	1032	1032	30	57% (17)	[196]
Aircraft carrier	382	382	238	18.5% (44)	[197]
Population of Vo', Italy	3276	2812**	73	39.7% (29)	[198]
		2343***	29	44.8% (13)	

* No absolute numbers reported.
** First survey.
*** Second survey two weeks later.

Table II
Clinical follow-up of asymptomatic carriers of SARS-CoV-2 in selected studies

Number of asymptomatic cases	Duration of follow-up	No symptoms or radiological findings during follow-up	Mild/moderate symptoms or radiological findings during follow-up	Severe COVID-19 pneumonia	Communicable period	Transmission to others	Reference
24	5–21 days	7 (29.2%)	17 (70.8%)*	0	Up to 29 days	One case caused three infections in the family, one of them severe	[72]
55	Unknown	0	53 (96.4%)**	2 (3.6%)**	3–20 days	Unknown	[199]
1 (6-month-old child)	17 days	1 (single transient temperature of 38.5°C)	0	0	16 days	Unknown	[200]
13	14 days	10 (77%)	3	0	Up to 12 days	Unknown	[201]

* Symptom onset one to three days after diagnosis.
** Symptom onset one to seven days after diagnosis.

systematic meta-analysis of different cohort studies observed that asymptomatic patients with COVID-19 seems to correlate with young age and social activity [76,77]. In particular, future studies aiming to understand the contribution of young patients such as children to asymptomatic transmission of SARS-CoV-2 should be prioritized [78]. In summary, the prevalence of asymptomatic SARS-CoV-2 infection and duration of pre-symptomatic infection are not well understood, as asymptomatic individuals are not routinely tested. Studies on the immune response of asymptomatic carriers are lacking, which could contribute to a better characterization of the protective factors under natural conditions [79].

Viral sources

Several sources have been described that could possibly be involved in SARS-CoV-2 transmission based on the detection of viral RNA. These include the respiratory tract, air contamination, the gastrointestinal tract, eyes, inanimate surfaces, PPE, pets, and rather less likely blood and the urinary tract.

Respiratory tract

SARS-CoV-1 has been frequently associated with droplet-based transmission [80,81]. Likewise, person-to-person transmission has been assumed for SARS-CoV-2 very early [21]. Importantly, a more efficient transmission of SARS-CoV-2 compared with SARS-CoV-1 has been suggested, due to active pharyngeal viral shedding while symptoms are still mild and typical of upper respiratory tract infection [7]. Table III summarizes the frequency and magnitude of SARS-CoV-2 viral RNA loads in respiratory tract samples obtained from COVID-19 patients.

The viral RNA load with SARS-CoV-2 can be as high as 11.1 $\log_{10}$ cpm (Table III). It seems to be particularly high in the early and progressive stage of disease [16] or two days before and one day after symptom onset [82]. However, in some cases RNA could still be found up to 51 days after the first positive test with negative results in between [15,83]. Influenza A virus RNA has even been released for up to 70 days with negative results in between although infectious virus was only detected for 5 days after symptom onset [84]. Age was also associated with high viral RNA load [15]. Most studies observed decreased viral RNA loads over time [5,7]. One study shows that SARS-CoV-2 was detected by culture in 19 of 25 clinical samples (nasopharyngeal swab) from COVID-19 patients [6]. The viral RNA load detected in the asymptomatic patient was similar to that in the symptomatic patients, which suggests the transmission potential of asymptomatic or minimally symptomatic patients [5]. It is important to differentiate between detection of RNA and the isolation of infectious virus in cell culture. PCR for RNA of SARS-CoV-2 does not distinguish between infectious virus and non-infectious nucleic acid. Thus, interpretation of duration of viral shedding and infection potential should be based on viable virus from cell culture and needs to be carefully evaluated when solely based on PCR results.

Transmission via droplets and aerosols

A strict distinction between droplet versus airborne transmission routes for infections is not possible [85]. Virus

Table III
Frequency and magnitude of SARS-CoV-2 viral RNA load in respiratory tract samples obtained from COVID-19 patients in selected studies

Number of COVID 19 patients	Respiratory tract symptoms	Viral RNA load	Additional information	Reference
76	74 with symptoms (97.4%) 2 without symptoms (2.6%)	4.2 log_{10} cps* (sputum) 3.4 log_{10} cps* (throat) 2.8 log_{10} cps* (nasal)	Viral RNA load high in early and progressive stage of COVID-19	[16]
9	Not described	5.5—5.8 log_{10} cps* (pharyngeal swab) 6.8 log_{10} cpm* (sputum)	Lower viral RNA load in whole swab samples after day 5; infectious virus isolated by culture was only detected during the first week of symptoms (16.7% of swab samples; 83.3% in sputum samples); no isolates were obtained from samples taken after day 8 in spite of ongoing high viral RNA loads	[7]
6	5 with symptoms (83.3%) 1 without symptoms (12.7%)	1.0—4.0 log_{10} cpc (nasopharyngeal swab) 1.0—3.0 log_{10} cpc (nasopharyngeal swab)	Viral secretion stopped after 5—17 days (median: 11 days)	[202]
5	All with symptoms	1.0—7.4 log_{10} cpc (nasopharyngeal swab)	Viral RNA load decreased over time; 1 patient with virus detection after 24 days (death of patient)	[11]
23	All with symptoms	4.1—7.0 log_{10} cpm (posterior oropharyngeal saliva)**	Old age was associated with high viral RNA load; salivary viral RNA load was highest during the first week after symptom onset; one patient had viral RNA detected for up to 25 days after symptom onset	[15]
15	All with symptoms	4.6 log_{10} cpm (respiratory tract specimen)	None	[152]
1	With symptoms	6.5 log_{10} cpm (pooled nasopharyngeal and throat swabs) 6.8 log_{10} cpm (sputum)	None	[95]
82	With symptoms	2.8—11.1 log_{10} cpm (1 nasal swab, 67 throat swabs and 42 sputum)	Median in sputum: 5.9 log_{10} cpm Median in throat samples: 4.9 log_{10} cpm	[13]
2	All with symptoms	4.7—7.7 log_{10} cpm (naso- and oropharyngeal swabs) 5.6—7.0 log_{10} cpm (sputum)	None	[203]
18	17 with symptoms (94.4%) 1 without symptoms (5.6%)	Up to 7.2 log_{10} cpm (nasal and throat swabs)	Viral RNA load decreased over time	[5]

cpc, copies per 1000 cells; cpm, copies per mL; cps, copies per whole swab or sample.
* Mean.
** Three patients with negative RNA test in saliva.

transmission via droplets and aerosols enables many viruses to spread efficiently between humans [86]. Airborne transmission is defined as the transmission of infection by expelled particles of comparatively small size and which can remain suspended in air for long periods of time [87]. The World Health Organization uses a particle diameter of 5 μm to delineate between airborne ($\leq$5 μm) and droplet (>5 μm) transmission [88]. Transmission of infectious diseases by the airborne route is dependent on the interplay of several factors, including particle size (i.e. particle diameter) and the extent of desiccation [87]. Particle desiccation is a critical variable and depending on environmental factors as even large, moisture-laden droplet particles desiccate rapidly [87]. For example, Wells showed that particles begin desiccating immediately in a rapid fashion upon air expulsion: particles up to 50 μm can desiccate completely within approximately 0.5 s [89]. Rapid desiccation is a concern because the smaller and lighter the infectious particle, the longer it will potentially remain airborne. Hence, even when infectious agents are expelled from the respiratory tract in a matrix of mucus and other secretions, causing large, heavy particles, rapid desiccation can lengthen the time they remain airborne (the dried residuals of these large aerosols, termed droplet nuclei, are typically 0.5—12 μm in diameter) [87]. Of further concern, very large aerosol particles may initially fall out of the air only to become airborne again once they have desiccated [87]. One of the challenges facing practitioners, particularly in an enclosed building, is that even large-sized droplets can remain suspended in air for long periods. The reason is that droplets settle out of air on to a surface at a velocity dictated by their mass [87]. If the upward velocity of the air in which they circulate exceeds this velocity, they remain airborne. Hence, droplet aerosols up to 100 μm diameter have been shown to remain suspended in air for prolonged periods when the velocity of air moving throughout a room exceeds the terminal settling velocity of the particle [87].

Respiratory virus shedding can occur via sneezing, coughing or talking. Sneezing distributes approximately 40,000 particles (droplets or airborne micro-organisms) per sneeze, coughing approximately 710 particles per cough, and talking approximately 36 particles per 100 words [87]. Using highly sensitive laser light scattering observations a recent study describes that loud speech can emit thousands of oral fluid droplets per second [90], indicating that normal speaking may also contribute to virus transmission in stagnant air. Most of the 40,000 large-droplet particles caused by a single sneeze will desiccate immediately into small, infectious droplet nuclei, with 80% of the particles being smaller than 100 μm [3]. The transmission of infectious diseases via airborne or droplet routes may further also depend on the frequency of the initiating activity. A single sneeze may produce more total infectious particles, while overall coughing may potentially be a more effective route of airborne transmission (e.g. during infection with Coxsackievirus A) [91]. Coronavirus-infected humans coughed on average 17 times over 30 min during exhaled breath collection [92]. Given that dry cough is also a common symptom of COVID-19 patients [93], it may therefore contribute to potential airborne transmission of this pathogen. In this context, airborne transmission has been considered to be possible in a cluster of infections in a restaurant with air conditioning [94].

Few studies are available that evaluated the role of air for transmission of SARS-CoV-2, most of them obtained in hospitals with COVID-19 patients. From the data shown in Table IV, viral copies were only detected in large air volumes of 9000 L with a larger proportion in intensive care units (ICUs) (35% detection rate) compared with general wards (12.5% detection rate). In smaller volumes such as 90 L, 1200 L or 1.5 m^3 no virus was detected. Even directly in front of a COVID-19 patient it was not possible to detect the SARS-CoV-2 RNA in the air [95]. The viral RNA loads of the first confirmed case were 3.3×10^6 copies per mL in the pooled nasopharyngeal and throat swabs and 5.9×10^6 copies per mL in saliva on the day of air sampling [95]. The air samples of 1000 L were collected at a distance of 10 cm at the level of patient's chin while the patient performed four different manoeuvres (i.e. normal breathing, deep breathing, speaking '1, 2, 3' continuously, and coughing continuously) while putting on and taking off the surgical mask were all undetectable for SARS-CoV-2 RNA [95]. Nosocomial transmission of SARS-CoV-2 by an airborne route has been described to be very unlikely [96]. Nonetheless, SARS-CoV-2 can remain infectious in air for 3 h measured in a Goldberg drum with a decline of viral load from 3.5 $\log_{10}$ to 2.7 $\log_{10}$ per litre of air [97]. In a subset of four study participants with a symptomatic seasonal coronavirus infection but without any coughing during the 30 min exhaled breath collection, no coronavirus RNA was detected in respiratory droplets or aerosols [92].

Other aspects influencing droplet or airborne transmission are temperature and humidity because they correlate with the spread of and deaths associated with COVID-19 [98–100]. In China, the number of confirmed cases increased with higher temperature and higher humidity in most of the provinces [101,102]. COVID-19 lethality significantly worsened (four times on average) with environmental temperatures between 4°C and 12°C and relative humidity between 60% and 80% [103]. Biktasheva *et al.*, however, described that the COVID-19 mortality correlates with low air humidity, probably caused by a lower resistivity of dry or very dry mucous membranes [104]. Huang *et al.* described that 60% of all COVID-19 cases are found in places with an air temperature between 5°C and 15°C [105]. In Brazil a 1°C increase in temperature has been associated with a decrease in confirmed cases of 8% [106]. In Wuhan and Xiaogan, temperature was the only meteorological parameter constantly but inversely correlated with COVID-19 incidence [107]. At low temperature and low humidity, droplets tend to remain suspended in air [108]. High relative humidity will increase the droplet sizes due to the hygroscopic growth effect, which increases the deposition fractions on both humans and the ground [109]. Overall, a seasonal pattern of COVID-19 is very likely.

SARS-CoV-2 aerosolized from infected patients and deposited on surfaces could remain infectious outdoors for considerable time during the winter in many temperate-zone cities, with continued risk for re-aerosolization and human infection [110]. Conversely, SARS-CoV-2 should be inactivated in the environment relatively fast during summer in many populous cities of the world, indicating that sunlight should have a role in the occurrence, spread rate, and duration of coronavirus pandemics [110]. Simulated sunlight has been described to rapidly inactivate SARS-CoV-2 [111,112].

Indoor transmission of SARS-CoV-2 is much more likely compared with outdoor transmission [113]. In a closed seafood market, the risk of a customer acquiring SARS-CoV-2 infection via the aerosol route after 1 h exposure in the market with one infected shopkeeper was about 2.23×10^{-5}. The risk rapidly decreased outside the market due to the dilution by ambient air and became below 10^{-6} at 5 m away from the exit [114]. Outdoor, these virus particles are very strongly diluted by the open air [115].

Gastrointestinal tract/stool

Some patients displayed diarrhoea at the beginning or during the course of infection suggesting that SARS-CoV-2 may also affect the gastrointestinal tract. Viral RNA was detected in a proportion between 9.1% and 100% in COVID-19 patients with up to 8.1 $\log_{10}$ viral copies per g (Table V). One study including 46 patients with 16 of them reporting gastrointestinal manifestations (35%) reported diarrhoea as the most common symptom (15%), followed by abdominal pain (11%), dyspepsia (11%), and nausea (2%) [116]. Analysing two groups of overall 12 patients, none of the stool samples resulted in successful virus isolation in cell culture, irrespective of viral RNA concentration [7,117]. In contrast, one study described the successful isolation of virus by cell culture from two of three patients [118]. Of note, another study showed higher viral RNA loads in faecal samples of mildly symptomatic or asymptomatic children compared with nasopharyngeal swabs [119]. These results indicate the possibility of faecal–oral transmission or

Table IV
Frequency of detection of SARS-CoV-2 RNA in air samples

Setting (country)	Placement of sampler	Sampled volumes of air	Detection of viral RNA	Additional information	Reference
Hospital rooms of confirmed COVID-19 patients (Iran)	2–5 m away from patients with severe and critical symptoms, height of 1.5–1.8 m	10 samples of 90 L	None	None	[204]
General ward with 8 air supplies and 12 air discharges per hour	General ward: different regions around the patient under the air inlet, and in the patient corridor	General ward: 16 samples of 9000 L	General ward: 2 samples (12.5%)	Highest detection rate in patients' rooms (8 of 18; 44.4%), followed by near air outlets (5 of 15; 33.3%) and doctors office area (1 of 8; 12.5%)	[138]
ICU with 12 air supplies and 16 air discharges per hour (China)	ICU: different regions near the air outlet, near the patients and around the doctors' office area	ICU: 40 samples of 9000 L	ICU: 14 samples (35%)		
Dedicated SARS-CoV-2 outbreak centre with 12 air exchanges per hour (Singapore)	In patient room and anteroom	6 samples of 1200 L	None	None	[186]
	Outside the patient room	6 samples of 1.5 m^3	None		
Isolation ward with 12 air exchanges per hour (China)	Negative pressure non-intensive care unit	6 samples of 1500 L	None	None	[205]
COVID-19 isolation rooms with 12 air exchanges per hour (Hong Kong)	Umbrella fitted with transparent plastic curtains as an air shelter to cover patients; 10 cm distance to patient's chin	10 samples of 1000 L	None	Direct sneezing on air filter: 1 of 5 samples positive; direct spitting on air filter: 5 of 5 samples positive	[136]
COVID-19 hospital (China)	Different departments in medical areas	44 samples of unknown volume	None	None	[206]
COVID-19 cases in isolation at home (Germany)	Middle of room most frequently used by residents	15 samples of 3000 L	None	None	[141]
Isolation rooms for COVID-19 patients (Ireland)	Surrounding of COVID-19 patients	16 samples of unknown volume	None	None	[207]
Intensive care units in designated COVID-19 hospital (China)	At the head of the bed within one meter of the patient's head	58 samples of 840 L* or 420 L**	1.7%	Detection near the head of the patient (1 sample)	[208]
Isolation wards in designated COVID-19 hospital (China)	Patient rooms and bathroom	38 samples of 840 L* or 420 L**	7.9%	Detection in bathroom (2 samples) and the patient room (1 sample)	[208]

ICU, intensive care unit.
* NIOSH sampler.
** DingBlue sampler.

Table V
Frequency and magnitude of SARS-CoV-2 viral RNA load in stool or rectal swab samples obtained from COVID-19 patients

Number of COVID 19 patients	Gastrointestinal symptoms	Viral RNA in stool or rectal swab samples	Viral RNA load	Additional information	Reference
59	15 with symptoms (25.4%) 44 without symptoms (74.6%)	9 patients (15.3%) 4 patients (9.1%)	4.7 log_{10} cpm	5.1 log_{10} cpm in patients with diarrhoea, 3.9 log_{10} cpm in patients without diarrhoea	[209]
5	1 with symptoms (20%) 4 without symptoms (80%)	2 patients (40%)	6.2–8.1 log_{10} cpg	Detection on days 2–19	[11]
15	Not described for the subgroup	4 patients (26.7%)	Not described	None	[15]
15	Not described	Number of patients not described	3.6 log_{10} cpm	None	[152]
17	Not described	9 patients (52.9%)	2.7–5.1 log_{10} cpm	None	[13]
4	Not described	4 patients (100%)	3–8 log_{10} cps	Virus isolation from stool samples was unsuccessful, irrespective of viral RNA concentration	[7]
46	16 with symptoms (35%), 30 without symptoms (65%)	2 patients (4%)	Ct values 29.9	None	[116]
38	Not described	8 patients (21%)	6.5 log_{10} cpm	Mean; virus isolation from stool samples was unsuccessful	[117]
28	Not described	12 patients (42.9%)	2.8–3.5 log_{10} PFU equivalent per mL	Virus isolation in 2 out of 3 patients successful	[118]
12	Not described	11 patients (92%)	4.1–10.3 log_{10} cpm	Children; median RNA load in fecal samples significantly higher than for nasopharyngeal swab specimens	[119]

cpg, copies per g; cpm, copies per mL; cps, copies per whole swab; PFU, plaque-forming units.

faecal–respiratory transmission through aerosolized faeces. Furthermore, the presence of SARS-CoV-2 RNA in bile juice was reported from one patient and it was speculated that RNA in faecal specimens may partly originate from bile juice [120]. Finally, a recent study suggested that detectable SARS-CoV-2 RNA in the digestive tract could be a potential warning indicator of severe disease [121], however further evidence will be needed.

Eyes

Transmission of SARS-CoV-2 through the ocular surface was considered to be possible [122]. Conjunctivitis has been reported in a patient in the middle phase of COVID-19, the conjunctival swab specimens remained positive for SARS-CoV-2 on 14 and 17 days after onset and were negative on day 19 [123]. Another study showed among 30 COVID-19 patients that the virus was detected in tears and conjunctival secretions only in the one patient with conjunctivitis [124]. Furthermore, in another group of 38 COVID-19 patients two of them were identified with positive findings for SARS-CoV-2 in their conjunctival as well as nasopharyngeal specimens, a total of 12 patients had ocular manifestations consistent with conjunctivitis, including conjunctival hyperaemia, chemosis, epiphora, or increased secretions [125]. In addition, no virus was detected on the conjunctiva in five other COVID-19 patients [11]. One patient was described with persistent conjunctivitis with viral RNA detection until day 27 after symptom onset and confirmation of infectious virus in the first RNA-positive ocular sample [126]. Even though the virus can be detected rarely in the conjunctival sac at very low levels [127,128], there is no evidence that it can replicate locally [129]. That is why the conjunctiva were considered not to be the preferred gateway into the respiratory tract [130].

A study analysed human post-mortem eyes for the expression of ACE2 (the receptor for SARS-CoV-2) and TMPRSS2. In all samples the expression of ACE2 and TMPRSS2 was detected in the conjunctiva, limbus, and cornea, with especially prominent staining in the superficial conjunctival and corneal epithelial surface [131]. In contrast, another study from Germany found no relevant conjunctival expression of the ACE2 receptor on mRNA and protein levels [132]. In summary, the detailed pathophysiology of ocular transmission of SARS-CoV-2 remains not completely understood [133] and both the presence of viral particles in tears and conjunctiva, and the potential for conjunctival transmission remains controversial [134]. In conclusion, spread of COVID-19 from ocular secretions cannot be ruled out but seems to be very unlikely.

Inanimate surfaces

Indirect transmission of COVID-19 has been assumed to be possible via fomites although direct evidence is currently not available [135]. In hospitals some data were collected to describe the frequency of detection of SARS-CoV-2 RNA on inanimate surfaces in the immediate patient surroundings. The

Table VI
Frequency of detection of SARS-CoV-2 RNA on inanimate surfaces

Setting (country)	Types of sampled surfaces (*N*)	Proportion of virus detection	Mean virus concentration (log_{10} cps)	Reference
COVID-19 isolation room (Singapore)	Bedding, cot rail and table (1 m distance to bed)	100%	Ct values between 37.8 and 28.7	[210]
ICU with COVID-19 patients (China)	Computer mouse (8)	75%	4.4	[138]
	Floor (10)	70%	4.8	
	Air outlet filter (12)	67%	5.2	
	Trash can (5)	60%	4.5	
	Sickbed handrail (14)	43%	4.6	
Dedicated SARS-CoV-2 outbreak centre (Singapore)	Room C: 26 surfaces (28 swabs) in a patient room before routine cleaning with sodium dichloroisocyanurate (0.5% on high touch surfaces, 0.1% on floors)	61%	Unknown	[186]
	Room B: 26 surfaces after routine cleaning	0%		
	Room A: 26 surfaces after routine cleaning	0%		
Surfaces in 27 hospital rooms of COVID-19 patients (Singapore)	Various surfaces (245)	56.7%*	Unknown	[211]
Isolation rooms for COVID-19 patients (Ireland)	Various surfaces in isolation rooms (26)	42.3%	Unknown	[207]
COVID-19 isolation ward (China)	112 surfaces in patient rooms and the toilet area at least 4 h after first daily surface disinfection with 0.2% chlorine solution	39.3%	Unknown	[205]
Centralized quarantine hotel (China)	Various surfaces (22)	36.4%	Ct values between 28.8 and 37.6	[212]
General ward with COVID-19 patients (China)	Sickbed handrail (10)	20%	4.0	[138]
	Doorknob (12)	8%	3.5	
	Floor (12)	8%	2.8	
	Air outlet (12)	0%	–	
COVID-19 hospital (China)	200 samples from various surfaces frequently touched by patients or healthcare workers	19.0%	Unknown	[206]
Clinical microbiology laboratory (France)	22 samples from various surfaces	18.2%	Unknown	[213]
Intensive care unit and isolation ward (South Korea)	57 surfaces in patient rooms, the ante room, the floor of an adjacent common corridor and the nursing station 1–72 h after last disinfection	17.5%	Unknown	[214]
Surfaces frequently touched by COVID-19 patients (Korea)	Surfaces in a rehabilitation centre and an apartment building complex (12)	16.7%**	Unknown	[215]
	Surfaces in hospitals (68)	0%***		
Different wards in grade III hospital (China)	626 samples from surfaces on different wards	13.6%	Unknown	[216]
Regular 4-bed rooms used for asymptomatic COVID-19 patients (South Korea)	22 surfaces in patient rooms, the ante room, the floor of an adjacent common corridor and the nursing station 184 h after last disinfection	13.6%	Unknown	[214]
COVID-19 cases in hospitals (Italy)	Various surfaces (26)	7.7%****	Unknown	[142]
COVID-19 isolation ward (China)	Various surfaces; routine daily disinfection with 0.1% chlorine dioxide (84)	7.1%	Unknown	[137]

Table VI (*continued*)

Setting (country)	Types of sampled surfaces (*N*)	Proportion of virus detection	Mean virus concentration (log_{10} cps)	Reference
COVID-19 isolation rooms (Hong Kong)	377 surfaces in patient rooms before daily disinfection with 0.1% sodium hypochlorite	5.0%	2.0—5.0 log cpm	[136]
COVID-19 cases in isolation at home (Germany)	Surfaces in 21 households (119)	3.4%****	Unknown	[141]
Dedicated general ward for COVID-19 cases (Singapore)	Various high touch surfaces in the patient surrounding and toilet area prior to terminal cleaning (445)	2.2%	Unknown	[217]
Intensive care unit and ordinary ward with COVID-19 cases (Taiwan)	144 samples from 16 different surfaces	1.4%*****	Ct values between 30.4 and 31.8	[218]
Designated COVID-19 hospital (China)	Various surfaces on isolation ward (144)	1.4%	Ct values between 38.6 and 44.9	[208]
COVID-19 patient room	Bench, bedside rail, locker, bed table, alcohol dispenser and window bench (unknown)	1 positive sample on window bench	2.8 log_{10} cpm	[95]
COVID-19 ward (Italy)	Various surfaces considered as high risk for contamination; routine daily disinfection with 0.1% sodium hypochlorite as free chlorine	0%	—	[187]
COVID-19 patient rooms (Japan)	15 surfaces in close contact with the patient and medical staff after surface disinfection	0%	—	[219]
Home of an asymptomatic quarantined SARS-CoV-2-carrier with persistently high viral loads (Korea)	Surfaces in household (12)	0%	—	[220]
COVID-19 isolation ward (China)	Various surfaces; routine daily disinfection with 0.1% chlorine dioxide (36)	0%	—	[221]
Designated COVID-19 hospital (China)	Various surfaces on intensive care units (160)	0%	—	[208]

cpm, copies per mL; cps, copies per swab.
* Proportion of room with at least one environmental surface contaminated.
** Door handles.
*** After cleaning and disinfection.
**** Detection of infectious SARS-CoV-2 was attempted in all samples and was consistently negative.
***** Only on ventilator tubing before HME filter.

detection rate was variable on ICU surfaces (0—75%), in isolation rooms (1.4—100%) and on general wards (0—61%). The mean virus concentrations per swab were 4.4—5.2 log_{10} on ICUs and 2.8—4.0 log_{10} on general wards. A positive correlation between patient viral RNA load and positivity rate of surface samples was described [136]. However, on cleaned and disinfected surfaces viral RNA could mostly not be detected (Table VI). Detection of viral RNA on the floor is indicative for sedimentation of contaminated droplets.

Surfaces outside the COVID-19 patient room were also investigated. On ICU the virus was rarely detected as 'weak positive' on the floor and on door knobs in three buffer rooms, six dressing rooms and a nurse station (six of 84 samples; 7.1%) [137]. On the general ward the virus was rarely detected on the patient floor (23 samples; one 'weak positive' result on the computer mouse or keyboard) and never detected on doorknobs and the floor in three buffer rooms and five dressing rooms (52 samples) [138]. Viral RNA could be detected even 28 days after discharge of COVID-19 on surfaces of pagers and in drawers of the isolation wards. The relevance of this finding, however, is not clear because it is not known if infectious virus was present at that time [139].

In a microbiology laboratory the detection rate on surfaces was 18.2%. In the domestic environment of SARS-CoV-2 carriers, the detection rate on surfaces was overall low (0—3.4%; Table VI).

It has to be mentioned that in most studies only PCR was performed for RNA. But detection of viral RNA on surfaces does not provide any information about viral infectivity or viability [140]. New findings from a COVID-19 cohort in Gangelt, Germany, and with cases in Italy provide data on the detection of infectious SARS-CoV-2 on surfaces. Although viral RNA was detected in 3.4% of 119 surface samples in 21 households of confirmed COVID-19-cases and on 7.7% of sampled surfaces around COVID-19-cases in Italy, infectious SARS-CoV-2 was not found in any sample [141,142]. Similar findings were described with SARS-CoV and influenza-virus. In Canada, a total of 85 samples from inanimate surfaces were taken in a SARS-hospital. Viral SARS-CoV RNA was present in 5.6% of samples, but none of the samples revealed infectious virus [143]. In Thailand and Taiwan, RNA of SARS-CoV was detected on 27.7% of 94 surface samples in a SARS-hospital or in a SARS-ward; in none of the samples was infectious SARS-CoV found [144]. Similar data were reported from 90 households with proven H1N1 influenza virus infections in children. Viral RNA was detected on 17.8% of inanimate surfaces but virus could never be cultured [145].

In cell culture studies, SARS-CoV-2 has been described to remain infectious on stainless steel and plastic for three to four days, on glass and banknotes for two days, on wood for one day, all with a decrease of viral infectivity with time [97,146]. In the close surrounding of COVID-19 patients in hospitals SARS-CoV-2 RNA is detected more frequently compared with surfaces outside the patient rooms but samples were so far consistently negative for infectious virus. Whether infectious SARS-CoV-2 may be detected in a relevant amount on various surfaces in public when only a short exposure to potentially infected, may be even asymptomatic people exists, is currently unknown but very unlikely. Surfaces in air planes or trains in coughing or sneezing distance for potentially infected long-distance travellers may theoretically have a higher risk for contamination.

PPE

The RNA of SARS-CoV-2 has so far mainly been found on PPE used by HCWs on ICU (0–50%), mainly on shoes and gloves. In other settings PPE was only very rarely contaminated with SARS-CoV-2 (Table VII). All studies performed PCR assays for SARS-CoV-2 RNA detection.

Blood

SARS-CoV-2 RNA has occasionally been detected in blood of COVID-19 patients, i.e. in one of five patients on days 7, 8, 9 and 12 after onset of disease [11], in five of 23 COVID-19 patients (21.7%) [15], in zero of 18 asymptomatic and symptomatic patients with SARS-CoV-2 infection [54], or in three of 307 samples (1.0%) obtained from 205 COVID-19 patients [147]. SARS-CoV-2 RNA can very rarely (in four of 2430 samples) be detected in plasma during routine screening of blood donors considered to be healthy population [148]. Detection of SARS-CoV-2 RNA in blood is considered a strong indicator for further clinical severity [149]. So far, no cases of transmission due to transfusion of blood products have been reported for SARS-CoV, MERS-CoV, or SARS-CoV-2, and clinically ill patients are not considered as blood donors [54]. Therefore, no immediate risk can be derived for the transfusion system [54]. Based on the existing evidence, transmission of COVID-19 by handling potentially contaminated blood products (laboratory technician) or by contact with blood, e.g., from a wound to intact skin is very unlikely.

Urinary tract

SARS-CoV-2 RNA has occasionally been detected in urine swabs from patients. In nine patients with confirmed SARS-CoV-2 infections, one of the patients was positive for viral RNA in urine [150]. This observation is supported by observations among 12 SARS-CoV-2 positive children with two of them positive for viral RNA in urine (17%) [119]. Importantly, infectious virus could be detected from urine in one COVD-19 patient [151]. However, other studies with a total of 47 patients [7,15,152] failed to detect SARS-CoV-2 RNA in urine. These data indicate that urine might be a potential source of infection but further evidence is needed.

Semen

There is evidence that the main entry receptor of SARS-CoV-2, ACE2, is expressed in cells of the reproductive system [153,154]. However, one study with 23 COVID-19 patients in the acute (12 patients) and recovery phases (11 patients) failed to detect viral RNA in semen [155], indicating a low probability of sexual transmission through semen.

Breast milk

SARS-CoV-2 RNA has temporarily been detected in breast milk samples in one study in one of two infected mothers with approximately 10^5 viral copies per mL [156]. Similarly, the presence of viral RNA was reported in breast milk of an actively breastfeeding mildly symptomatic COVID-19 patient raising the possibility of a potential transmission from breast milk [157].

Pets

Thus far, no evidence for transmission of the virus from pet animals to humans exists [158]. However, Shi *et al.* reported that ferrets and cats were highly susceptible to SARS-CoV-2, while dogs had a low susceptibility and livestock including pigs, chickens, and ducks were not susceptible to the virus, under experimental conditions [159]. One of 22 cats (France) and two of 10 cats (Wuhan) of COVID-19 patients has been described to have a SARS-CoV-2 infection with mild respiratory and digestive symptoms whereas all 11 dogs (France) and eight of nine dogs (Wuhan) were SARS-CoV-2 and serologically negative [160,161]. Interestingly, viral transmission between cats has been observed [159]. Out of six naïve cats (three subadults and three juveniles), each exposed to a SARS-CoV-2 inoculated cat, transmission occurred in two cats (one cat of each age group). Similar findings were reported by Halfmann *et al.* [162]. This indicates that cats, being common companion animals, might theoretically transmit the virus to other animals and humans. However, there is so far no clear evidence that cat-to-human transmission of SARS-CoV-2 can occur.

Control of SARS-CoV-2 transmission

Several practices are recommended with the aim to limit further transmission of SARS-CoV-2 in clinical practice but also public settings. These include handwashing, hand disinfection, wearing of face masks and gloves, disinfection of surfaces and

Table VII
Frequency of detection of SARS-CoV-2 RNA on personal protective equipment (PPE) of healthcare workers

Type of ward (country)	Types of sampled surfaces (*N*)	Proportion of virus detection	Mean virus concentration (log_{10} cps)	Reference
ICU with COVID-19 patients (China)	Shoe sole (6)	50%	4.5	[138]
	Glove (4)	25%	4.5	
	Sleeve cuff (6)	17%	4.9	
	Face shield (6)	0%	–	
General ward with COVID-19 patients (China)	Shoe sole (3)	0%	–	[138]
	Glove (3)	0%	–	
	Sleeve cuff (3)	0%	–	
	Face shield (3)	0%	–	
COVID-19 isolation room (Singapore)	Face shield (1)	0%	–	[210]
	N95 mask (1)	0%	–	
	Waterproof gown (1)	0%	–	
COVID-19 isolation room (Singapore)	Different surfaces from PPEs (30)	0%	–	[222]
COVID-19 isolation room (Singapore)	Different surfaces from PPEs (10)	10% (front of shoes)	Ct value of 38.96*	[186]
Different wards in grade III hospital (China)	Hand sanitizer dispenser (59)	20.3%	Unknown	[216]
	Glove (78)	15.4%		
	Eye protection or face shield (58)	1.7%		
COVID-19 negative pressure isolation room (South Korea)	Different surfaces from PPEs (133)	11.3%**	Unknown	[223]

cps, copies per swab.
* Indicating a low viral RNA load.
** Mainly on the top of the head and the foot dorsum.

physical distance. Based on an integrated theoretical and statistical analysis of the influence of individual variation in infectiousness on disease emergence it has been suggested that individual-specific control measures outperform population-wide measures [35].

Handwashing

A hand soap solution (1:49) has been described to have some effect ($\geq$3.6 $\log_{10}$ reduction of viral infectivity) against SARS-CoV-2 in 5 min [146]. For HCWs handwashing is only useful when hands are visibly soiled [163]. Although SARS-CoV-2 has never been detected on hands of the public population yet, it seems reasonable to assume that the hand contamination by droplets from others may take place in the public with an unknown viral load. Apart from avoiding hand—face contacts in general, handwashing is the first choice for the decontamination of hands, especially after returning home from public places with many close contacts with potentially infected people.

Hand disinfection

Ethanol and iso-propanol inactivate SARS-CoV-2 at concentration between 30% and 80% (both v/v) in 30 s [164]. Both WHO-recommended hand rubs based on 75% iso-propanol or 80% ethanol (both v/v) also inactivate SARS-CoV-2 in only 30 s [164]. Similar results were obtained with a propanol-based hand rub against SARS-CoV [165]. On clean hands use of an alcohol-based hand rub is first choice in healthcare for the decontamination of hands due to the better activity against nosocomial pathogens including bacteria and yeasts and a better dermal tolerance [163]. It may also be useful for COVID-19 patients, e.g., before leaving the patient's room for examinations. In this situation it is reasonable to recommend a hand disinfection in order to reduce potential transmission by direct hand contacts. The routine use of alcohol-based hand rubs for the general population should be discouraged, since there are currently no clear indications when to use them. It may be useful if a contamination of hands with SARS-CoV-2 is likely and a handwashing facility is not available. Otherwise the widespread use of alcohol-based hand rubs may even enhance the shortage of the products in patient care which should be avoided by all means [166].

Face masks

Inadequate PPE including facemasks at the beginning of the epidemic in China has resulted in infections and deaths among HCWs [167,168]. Unprotected patient care with long and close contacts was also later a major risk for HCWs to acquire COVID-19 [169]. In COVID-19 cases face masks can at least reduce the viral spread. In 17 individuals with a symptomatic seasonal coronavirus infection a surgical face mask was able to reduce the proportion of viral RNA detection in droplets from 30% to 0% and in aerosols from 40% to 0% during 30 min exhaled breath collection, suggesting a protective effect when worn by infected patients [92]. In another study, four COVID-19 patients coughed five times in front of a Petri dish (20 cm distance) with a surgical mask, a cotton mask or without a mask. Without a mask 2.6 $\log_{10}$ viral copies per mL were detected, with a surgical mask it was 2.4, and with a cotton mask 1.9 $\log_{10}$ viral copies per mL [170]. Household transmission was more likely when the primary case and other household members did not wear a mask at home resulting in the possibility of unprotected transmission [171]. Data on a protective effect of face masks when only worn by healthy subjects in an endemic COVID-19 setting are not available. Despite these results it was shown in South Korea that none of 35 HCWs with close contacts to a COVID-19 patient developed symptoms or were PCR positive in the nasopharynx although they only wore a surgical mask for more than 10 min during activities including aerosol-generating procedures such as intubation [172]. In addition, one study could show that a four-day surgical mask partition between cages reduces the risk of non-contact transmission between artificially infected and naïve golden Syrian hamsters [173].

Importantly, a used face mask worn by a SARS-CoV-2 spreader will be contaminated. After only five coughs all surgical or cotton face masks worn by COVID-19 patients were contaminated on the outer surface whereas samples from the inner surface were mostly negative [170]. Chin *et al.* found that the virus can remain infectious or detectable for up to seven days on the outer layer of a surgical mask, on the inner layer for four days [146]. Although the results are only based on three independent triplicates, this finding should have implications for the re-use of face masks in a shortage situation [166].

Wearing a face mask is recommended for HCWs in case of suspected or confirmed COVID-19 patients [2,174] although it was described in Hong Kong that 11 of 413 HCWs had unprotected exposure to confirmed COVID-19 cases, none of these were infected [95]. Wearing a face mask may also be useful for HCWs when mild respiratory symptoms occur because in the Netherlands 4.1% of such HCWs were positive for SARS-CoV-2 [175]. Even universal masking in hospitals by HCWs has been proposed although the expected effect was described as marginal [176].

Suspected and confirmed COVID-19 cases should wear a face mask to prevent the spread of infectious droplets [2].

So-called mass masking has been proposed as a considerable option [177,178]. Many countries have recommended or legally ordered the use of fabric masks or face coverings for the general public. The WHO, however, acknowledged that the widespread use of masks by healthy people in the community setting is not yet supported by high quality or direct scientific evidence and that there are potential benefits and harms to consider [179]. But in areas of known or suspected widespread community transmission and limited or no capacity to implement other containment measures, governments should encourage the general public to wear masks in specific situations and settings [179]. Some recent studies suggest that general face mask usage by the healthy population in the community reduces the risk of transmission [180,181]. But in order to evaluate only the effect of masks worn by healthy people in the community on the prevention of transmission in a country or region, some relevant variables with a proven impact on transmission should have been considered for the study period: the seasonal effect on the incidence (similar weather conditions), the main mode of transmission during the period of observation (mainly local clusters or mainly transmission in buildings or mainly transmission in public), the total number of new cases in the observation period (mass masking in a region with one new case per day may have a different effect compared with a region with 10.000 new cases per day) and the extent of community lockdown (the fewer people there are out in public, the less likely a protective effect of general masks can be expected). In an endemic population scenario without restrictions regarding physical distance and close or long face-to-face contacts it may indeed be useful, especially for the part of the population which has a high risk for a severe COVID-19 infection. It is, however, a controversial debate among the scientific community if any additional protective effect by mass masking is expectable if a minimum distance between people is assured (e.g., 2 m) and contacts are only of short duration.

Gloves

Gloves can partially prevent the contamination of the hands with specific pathogens or all types of bioburden [182]. However, at the same time wearing gloves is associated in hospitals with a lower compliance with hand hygiene [183,184]. Use of gloves is recommended for HCWs in specific patient care activities, e.g., when soiling of the hands is expected and when caring for COVID-19 patients [2,163]. Whether there is any protective effect by wearing gloves by the general population in public is speculative. One aspect is that wearing gloves may result in more awareness to reduce face–hand contacts. And yet it seems reasonable not encourage the general population to routinely wear gloves in public. Even if a hand contact yields a transient contamination with SARS-CoV-2 on the hands it does not make a difference if the virus is found on the bare or gloved hand; the essential preventive measure in this case is to avoid hand–face contacts and to wash hands when returning from being out in public. The resident hand flora is even able to provide some colonization resistance in contrast to the glove [185]. If wearing gloves by the general population has a similar effect on hand hygiene compliance as it has been described for HCWs, wearing gloves in public may even have the unwanted effect of less handwashing potentially increasing the risk of transmission via hands.

Disinfection of surfaces with multiple hand contacts

Some surface disinfectant agents have been described to inactivate SARS-CoV-2 in 30 s such as ethanol and iso-propanol (30–80%, v/v) [164]. In 5 min, household bleach (1:49 and 1:99) and 0.1% benzalkonium chloride were also very effective against SARS-CoV-2 [146]. Limited data from surface samples in COVID-19 settings support their efficacy [186,187]. In healthcare settings routine cleaning and disinfection of surfaces with which the patient is in contact is recommended [2]. Thus far, no studies were reported to address whether SARS-CoV-2 (viral RNA or infectious virus) may be found on public inanimate surfaces. Disinfection of surfaces in a household with chlorine- or ethanol-based products can reduce the risk of transmission when the primary case has diarrhoea [171]. The frequent use of household disinfectants also results in a remarkable increase of exposures reported to US poison centres, especially via ingestion in the age group between 0 and 5 years [188]. General disinfection of frequently touched surfaces in public such as shopping carts or door handles is, however, unlikely to add any protective value because even in COVID-19 wards inanimate surfaces were mainly contaminated in the permanent and immediate surrounding of symptomatic patients (detection of viral RNA, not of infectious virus) and only rarely one room away [138] suggesting that the risk of finding SARS-CoV-2 on frequently touched surfaces in public is low. Future research will hopefully clarify the role of public inanimate surfaces for the spread of SARS-CoV-2.

Physical distance

Close and long contacts are probably the main risk for transmission of SARS-CoV-2 from asymptomatic or symptomatic patients to healthy people as shown in clusters in families, a cruise ship, hospitals and nursing homes [189]. The mode of transmission is very likely by droplets during coughing, sneezing or talking. The risk of long and close contacts is supported with experimental data obtained with eight Syrian hamsters inoculated with 10^5 viral copies in 100 μL intranasally. Twenty-four hours later each hamster was transferred to a new cage with one naïve hamster as close contact. SARS-CoV-2 was detected in nasal secretions, trachea and lung after 4 days in all naïve contact hamsters [190].

Physical distancing is another option to slow down the spread of SARS-CoV-2. Early data from China suggests that quarantine, physical distancing, and isolation of infected populations can flatten the epidemic [191]. Thus far, there are no 'real-life' data which provide conclusive evidence regarding effectiveness of physical distancing interventions. However, in a simulation model, the likelihood of SARS-CoV-2 human-to-human transmission in a Singaporean population was predicted [192]. They could demonstrate that the combined intervention, in which quarantine, school closure, and workplace distancing were implemented, was the most effective compared with the baseline scenario of no interventions, which reduced the estimated median number of COVID-19 infections by 99.3% when R 0 was 1.5, by 93.0% when R 0 was 2.0, and by 78.2% when R 0 was 2.5 [192]. Nevertheless, an evaluation of the effect of physical distancing alone is currently not possible. Maintaining a physical distance of at least 1 m from other individuals is regarded as one of the most effective preventive measures by the WHO [193].

Conflict of interest statement
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