ARHAI Scotland

Antimicrobial Resistance and Healthcare Associated Infection

NHS National Services Scotland

Rapid review of the literature: Assessing the infection prevention and control measures for the prevention and management of COVID-19 in health and care settings

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Version history

Version	Date	Summary of changes
1.0	19/3/2020	Assessment of the emerging COVID-19 evidence base, includes literature identified up to 16 March 2020.
1.1	3/4/2020	Assessment of the emerging COVID-19 evidence base, includes literature identified up to 30 March 2020.
1.2	20/4/2020	Assessment of the emerging COVID-19 evidence base, includes literature identified up to 13 April 2020.
3.0	15/5/2020	Monthly assessment of the emerging COVID-19 evidence base, includes literature identified up to 11 May 2020.
4.0	24/6/2020	Monthly assessment of the emerging COVID-19 evidence base, includes literature identified up to 15 June 2020.
5.0	23/7/2020	Monthly assessment of the emerging COVID-19 evidence base, includes literature identified up to 20 July 2020
6.0	2/9/2020	Monthly assessment of the emerging COVID-19 evidence base, includes literature identified up to 31 August 2020
7.0	2/10/2020	Monthly assessment of the emerging COVID-19 evidence base, includes literature identified up to 28 September 2020
8.0	05/11/2020	Monthly assessment of the emerging COVID-19 evidence base, includes literature identified up to 02 November 2020
9.0	04/12/2020	Monthly assessment of the emerging COVID-19 evidence base, includes literature identified up to 30 November 2020
10.0	15/01/2021	Monthly assessment of the emerging COVID-19 evidence base, includes literature identified up to 05 January 2021
11.0	05/02/2021	Monthly assessment of the emerging COVID-19 evidence base, includes literature identified up to 01 February 2021
12.0	12/03/2021	Monthly assessment of the emerging COVID-19 evidence base, includes literature identified up to 01 March 2021
13.0	09/04/2021	Monthly assessment of the emerging COVID-19 evidence base, includes literature identified up to 29 March 2021
14.0	07/05/2021	Monthly assessment of the emerging COVID-19 evidence base, includes literature identified up to 26 April 2021

Contents

1. Aim

To provide a rapid review of the scientific evidence base to inform the infection prevention and control measures required for the prevention and management of COVID-19 in health and care settings.

2. Objectives

Objectives for the rapid review were to establish the following:

- The epidemiology of COVID-19;
- The personal protective equipment (PPE) requirements;
- The requirements for hand hygiene;
- The environmental survivability of COVID-19;
- The requirements for cleaning/decontamination of the care environment;

3. Methodology

The methodology for this rolling rapid review was developed to ensure frequent and timely assessment of the emerging evidence base could be provided.

Academic databases (Medline and Embase) were first searched on 5th March 2020 to identify relevant literature (see Appendix 1 for search strategies). Searching was also conducted on the pre-print database, medRxiv (via NIH icite). Additional grey literature searching was conducted which included searching online resources from the World Health Organization (WHO), the US Centers for Disease Control and Prevention (CDC), the European Centre for Disease Prevention and Control (ECDC), Public Health England, UK, Scottish, Canadian and Australian Government guidance, the UK Scientific Advisory Group for Emergencies (SAGE), the Novel and Emerging Respiratory Virus Threats Group (NERVTAG).

Studies were excluded if they were published pre-2000, if they were published in non-English language and if they were animal studies.

Inclusion criteria was kept broad owing to SARS-CoV-2 being a novel pathogen, any study design was considered. Screening was undertaken by two reviewers, any uncertainty over the relevance of an article was decided by agreement between the two reviewers. As this was a rapid review, evidence was critiqued but not formally graded with the use of an appraisal tool, meaning that graded recommendations were not feasible.

The SIGN50 critical appraisal system is used for ARHAI Scotland systematic reviews and while time constraints meant individual studies were not entered into SIGN50 checklists for this rapid review, the SIGN50 principles were applied to critical analysis of the evidence base and data extraction from studies was entered directly into evidence tables developed for the rapid review.

3.1 Evidence updates

The emerging evidence base on COVID-19 is rapidly changing. To account for this, published literature is screened on a weekly basis and weekly evidence updates produced. Updates to the rapid review will be made on a monthly basis, or if the evidence base indicates that a change to recommendations is required.

4. Epidemiology

4.1 Transmission routes

Early analysis of the transmission of COVID-19 was thought to occur mainly via respiratory droplets[1-10] generated by coughing and sneezing, through direct contact[1, 3, 6-11] and indirect contact with contaminated surfaces.[1, 6, 7, 9, 10] These transmission routes were supported by early National[12-14] and international guidance.[15, 16] The World Health Organization (WHO) in a scientific brief published July 2020 supported that the main mode of transmission was via respiratory droplets, which are expelled when an infected person coughs, sneezes, talks or sings.[17] Transmission through contact with contaminated surfaces (fomite transmission) is considered possible due to the presence of COVID-19 viral RNA on surfaces (see section 7 – survival in the environment) however there has so far been no published evidence to demonstrate singularly in real-life scenarios, as it is impossible to separate the contribution from other transmission modes.

As the pandemic has progressed, there have been growing calls to acknowledge a potential airborne transmission route. The European Centre for Disease Prevention and Control (ECDC) describe transmission as occurring via respiratory droplets, either by being inhaled or deposited on mucosal surfaces, including aerosols produced when coughing and speaking, however acknowledge that the relative role of large droplet, aerosol and fomite transmission remains unclear.[18] The US Centers for Disease Prevention & Control (CDC) stated in a scientific brief published 5th October 2020 that airborne transmission may be possible under special circumstances, specifically: in enclosed spaces, during prolonged exposure to respiratory particles, and where there is inadequate ventilation or air handling.[19] The WHO published an updated scientific summary of COVID-19 transmission in December 2020, stating that outside of medical facilities, in addition to droplet and fomite transmission, aerosol transmission could occur in specific settings and circumstances, particularly in indoor, crowded and inadequately ventilated spaces, where infected persons spend long periods of time with others.[20] The CDC state that there are several well-documented examples in which transmission appears to have occurred over long distances or times, however the references provided in the report, which are largely from outbreak reports in overcrowded community settings (restaurants, recreation) do not provide clear evidence of 'traditional' airborne transmission (defined as long distance transmission of respiratory aerosols). The evidence base for possible human-human airborne transmission, as presented by the CDC, is largely from community settings.[21-23] Outbreak reports are, by their nature, prone to many methodological limitations (e.g. self-report bias, publication bias, lack of robust data) however continue to be the main source of evidence regarding transmission modes. In the absence of robust evidence for airborne transmission, a more accurate description of what might be facilitated in those specific circumstances as described by both the CDC and WHO is 'short-range aerosol' transmission, whereby poor ventilation combined with overcrowding/close contact in small spaces provide the conditions for respiratory aerosols to remain suspended in the air thus increasing the risk of transmission. The UK Scientific Advisory Group for Emergencies (SAGE) in April 2021 stated that evidence suggests airborne transmission is most likely in poorly ventilated spaces but that applying full conventional airborne precautions throughout a hospital is neither practical nor likely to be necessary.[24] Currently there is no clear evidence of 'traditional' long-range airborne transmission of SARS-CoV-2 from outbreak reports. From unpublished Scottish outbreak reporting from acute care settings it is clear there is large variation in the size and duration of outbreaks, with some units experiencing just a few cases per outbreak cluster and others in the double figures. Consistently large outbreaks might be expected with a predominantly airborne transmission mode however there are many confounding factors that could impact the transmission rate. Prolonged shedding in a patient could also theoretically maintain an

outbreak, inability of some patients to wear facemasks, breaches in control measures such as physical distancing, hand hygiene, adequate cleaning and PPE use and delays in recognising symptoms can also significantly contribute to the transmission rate. All of these have been reported consistently during outbreaks and are further fuelled by increasing inpatient numbers and staffing shortages. There are wards in which contact and droplet precautions were applied for managing COVID-19 patients with no onwards transmission. Without a detailed epidemiological investigation, ideally with whole genome sequencing, it is very challenging to obtain data from outbreak reports that provides reliable and valid assessment of the potential transmission modes.

It must be acknowledged that further research is required to determine the potential contribution of aerosol transmission of respiratory viruses, acknowledging a spectrum of particle sizes. This would include analysis of, for example, experimental studies that do not involve actual human-human transmission but demonstrate a theoretical aerosol 'potential'. These include experimental laboratory studies designed to assess visualisation of droplet expulsion from the human mouth/nose, mechanically-generated aerosol studies where the air is experimentally seeded with viral particles, animal studies involving an artificially infected donor and recipient, and air sampling studies where presence of viral RNA (and subsequent cell culture) is used as a proxy for transmission risk. These studies collectively demonstrate a potential for air-mediated transmission but are generally considered low quality evidence due to concerns regarding their validity and representativeness (particularly with regard to the animal studies).

Air sampling studies conducted in COVID-19 healthcare environments have shown mixed results. A number of international studies (South Korea, Ireland, China, Iran, Italy, Canada) returned negative results for the presence of viral RNA by RT-PCR in air samples collected from active air sampling[25-34] or settle plates[35] in ICUs, single patient rooms, multi-bed bays, general corridors, fever clinics, EDs, rooms of long term care facilities, treatment rooms and throat swab sampling rooms, and 'clean' areas.[36] In these studies, patients were often intubated, mechanically ventilated, on non-invasive ventilation or receiving high-flow nasal oxygen (HFNO). The distance between the air samplers and the patients varied from 0.6m to 5m. Symptom severity, number of days since symptom onset, and environmental ventilation provision in these studies also varied. There has been an attempt to assess the influence of ventilation on the observed outcomes of air sampling (and environmental sampling);[34] this is a methodologically challenging task with many confounding factors to account for.

Studies that have reported positive air samples are also heterogeneous in terms of patient symptoms, duration since symptom-onset, ventilation provision, and distance of sampler

placement from patients. Positive air samples have been reported in isolation rooms and corridors of COVID-designated hospitals,[37] airborne isolation rooms of general wards,[38, 39] PPE-removal rooms,[40-42] ICUs,[36, 41, 43, 44] hospital corridors,[36, 42] bays,[45] and single patient rooms.[45-48] Active air sampling in 2 Wuhan hospitals demonstrated positive results in PPE-removal rooms, which led the author to suggest resuspension of virus-laden aerosols from the surface of contaminated PPE was contributing to air contamination; very low/non-detectable concentrations of viral RNA was detected in COVID-19 ICUs.[40] Active air sampling in an ICU treating 15 patients with severe disease and in a general ward treating 24 patients with mild disease returned positive results in 35% of samples collected from the ICU and 12.5% of samples from the general ward.[43] A study at a hospital in China detected viral RNA in one out of 12 bedside air samples collected at a distance of 0.2 metres; breath condensate samples from the patient were also positive however it is not possible to distinguish droplet from airborne detection in this study, and there was no data provided regarding the clinical procedures conducted in the room before or during sampling.[49] Active air sampling in a London hospital detected viral RNA in samples from multiple patient areas however repeat sampling returned positive results in 3 areas only.[50] When testing was carried out in the presence of tracheostomies, only 1 of 8 samples was positive. One out of 12 active air samples taken from COVID-19 patient rooms in a hospital in Wuhan tested positive within 10cm of a patient undergoing endotracheal intubation for invasive mechanical ventilation.[46] Four out of 55 samples taken <1m from patients at 8 hospitals in England tested positive; 3 of the 4 patients were undergoing AGPs at the time (CPAP, non-invasive ventilation).[45] One study has demonstrated the presence of viral RNA in the filters of exhaust ducts located ~50 metres from COVID-19 patient rooms; samples were collected by placing cut sections of HEPA filter into viral transport medium.[51] Identification of viral RNA on air ducts/ventilation grilles has been highlighted as potentially indirect evidence of aerosol production, however unpicking the potential contributors to contamination in these studies is challenging.[52]

Notably, there is large heterogeneity in the sampling method employed in these studies, and no recognised standard for air sampling, which may impact the observed outcomes. The ventilation systems and modifications also differed significantly between settings. A major limitation in these studies is the lack of detail regarding the types, timing and duration of clinical procedures carried out, therefore limiting a full understanding of their potential impact on the observed sampling results. Positive air samples from ICUs/patient rooms may be a reflection of the higher aerosol risk that is related to aerosol-generating procedures (AGPs) that are conducted in these high risk clinical settings. Conversely, the observed negative air samples in some studies may be impacted by the ventilation provision, as a higher air change rate (the

number of air changes in the space per hour) has been shown to be associated with a lower infection risk in modelling studies. [53] A living systematic review assessing air sampling was unable to identify any pattern between the type of hospital setting (e.g. ICU versus non-ICU) and RT-PCR positivity in air samples.[54]

Few studies have tested viability of air samples. Four out of 6 samples taken from a single hospital room containing 2 COVID-19 patients at a hospital in Florida were positive; inoculation in Vero E6 cells showed cytopathic effect, suggesting viability.[55] Again, this study does not detail the types of patient care activities performed in these rooms. Most studies have been unable to identify viable virus or viral replication in air samples collected from hospital inpatient rooms.[39, 45, 47, 50, 56, 57] Viral culture is often used as a proxy for infectivity however there is no certainty that individuals with non-culturable samples are not infectious.

Aerosol-generating procedures

Aerosol-generating procedures have been associated with an increased risk of transmission of previous coronaviruses (SARS-CoV and MERS-CoV)[16, 58] and a number of AGPs (mostly airway management) have been implicated as risk factors for transmission of SARS-CoV-2 to health and care workers (HCWs)[9, 59] however attributing risk to specific procedures with any level of certainty is challenging. The concept of an 'aerosol generating procedure' arose following the study of SARS-CoV transmission events where it was observed that a pathogen, which was consistently associated with droplet or contact transmission, appeared to have the potential to infect HCWs via the airborne route during specific procedures. This is reflected in the World Health Organization's (WHO) definition of an AGP which states that AGPs create the potential for airborne transmission of infections that may otherwise only be transmissible by the droplet route.[60] It should also be recognised that as well as producing aerosols, these procedures produce a spectrum of droplet sizes including larger droplet particles.[61-63]

The WHO further defines an AGP as those procedures which result in the production of airborne particles (aerosols).[60] Particles which they describe as being <5 micrometres (μm) in size and as such can remain suspended in the air, travel over a distance and may cause infection if inhaled.[60] These particles are created by air currents moving over the surface of a film of liquid, the faster the air, the smaller the particles produced.[60] Using this definition there are potentially many medical or patient care procedures which could be classed as 'aerosol generating' but whether they lead to an increased risk of respiratory infection transmission is a different and important question. The 2014 WHO guidance is specific in its wording, outlining that '*some procedures potentially capable of generating aerosols are associated with increased risk of SARS transmission to health-care workers*' and they outline that, regarding pandemic

and epidemic prone acute respiratory infections, it is for these procedures that airborne precautions should be used.[60] Medical and patient care procedures should be assessed based not only on their capacity to generate aerosols but also on their ability to generate infectious aerosols and an association with relevant transmission events. For example, whilst it has been observed under experimental conditions using healthy volunteers that continuous positive airway pressure ventilation (CPAP) and high flow nasal oxygen delivery (HFNO) (both AGPs) may produce less aerosols than coughing, there was no assessment of the generation of infectious aerosols in these scenarios tested.[64] Health Protection Scotland conducted a review of the evidence base for a number of clinical procedures for their consideration as AGPs in relation to increased risk of respiratory infection transmission, in collaboration with the Department of Health and Social Care's New and Emerging Respiratory Virus Threat Assessment Group (NERVTAG).[65] Additional clarity was provided regarding dental procedures and surgical/post-mortem procedures; risk during dentistry is related to the use of high speed devices such as ultrasonic scalers and high speed drills. In surgery/post-mortem, risk is related to the use of high speed cutting if this involves the respiratory tract or paranasal tissues.

Variants of concern

In December 2020, a new SARS-CoV-2 variant (Variant of Concern (VOC) 202012/01, also known as B.1.1.7 lineage) was identified in the south west of England. B.1.1.7 differs by 29 nucleotide substitutions from the original Wuhan strain, having multiple spike protein mutations with one of the S-gene mutations deleting two amino acids at positions 69 and 70 causing a reproducible S-gene target failure (SGTF) in the Thermofisher TaqPath assay used in the UK Lighthouse laboratories.[66] The observed rapid increase in COVID-19 cases overall in the south west of England was temporally associated with the emergence of the new variant in this area in November 2020. SAGE/NERVTAG have stated there is 'high confidence' that this variant is spreading faster than other SARS-CoV-2 virus variants currently circulating in the UK, with apparent evidence that is consistent with an increase in transmissibility being a factor. Preliminary evidence suggested the possibility of lower Ct values in those infected with this variant, which is consistent with an increase in viral load, [67] however this has not been demonstrated in more recent studies. There is so far no evidence to suggest an increase in severity of symptoms or mortality associated with this new variant. There is no indication that the transmission modes have changed and therefore no changes required to the current IPC measures. Further information regarding the new variant(s) is provided in a separate ARHAI Scotland **rapid review.**

Conclusion:

- Transmission of SARS-CoV-2 is thought to occur mainly through close contact with an infectious individual, mediated by respiratory particles.
- Currently there is no clear evidence of 'traditional' long-range airborne transmission of SARS-CoV-2, however the contribution of air-mediated transmission, acknowledging a spectrum of droplet sizes, requires further research.

4.2 Clinical presentation

Whilst it is apparent that there is variation in the severity and range of symptoms experienced, the most frequently reported symptoms from case and cohort studies include fever and cough.[68-86] UK data also reflects this.[87, 88] Analysis of a large UK cohort of cases hospitalised between 6th February and 8th May (n=24,477) demonstrated that cough was the most prevalent symptom, followed by fever and dyspnoea.[89] Prevalence of individual symptoms varied with age, with fever being less marked at the extremes of age, and runny nose limited to mostly those aged <20 years, especially to those aged under 10 years. A core symptom set of fever, cough, and dyspnoea was identified, and accounted for the largest number of patients (n=9363, 36.%). This core symptom set was found to co-occur with additional symptoms in three patterns; 1) fatigue and confusion, 2) diarrhoea and vomiting, and 3) productive cough. Similar symptom patterns were observed in 4,445 patients from a study of self-reported symptoms of mild disease.[89] Anosmia and ageusia (loss of smell and taste), although more subjective, have also been reported[68, 90-94] and these symptoms were added to the UK's official list of symptoms in May. Amongst hospitalised paediatric and adolescent cases, the most frequently reported symptoms are also fever and cough.[95] This also appears to be the case in community cases, with runny nose also predominant, however the data is less reliable, being self-reported or reported by a family member.[96] Paediatric cases tend to have less severe disease, are hospitalised less frequently than adult patients and are less likely to be admitted to ICU.[97-104] Analysis of symptoms in 126 residents from 4 care homes in London found that early onset anorexia had the strongest independent association with a positive RT-PCR test; cough or shortness of breath were also significantly and independently associated, whilst fever, altered mental state, and diarrhoea were not.[105]

It is widely recognised that those individuals with underlying comorbidities (diabetes, cardiovascular disease, lung disease, cancer) have an increased risk of ICU admission and mortality.[106-112] Analysis of 36,398 COVID-19 patients demonstrated that 42.5% had one or

more pre-existing morbidity; the most common was hypertension (36.4%), cardiovascular disease (11.9%), and diabetes (22.0%) – mortality rate in the cohort was 14.5% (5,310/36,398).[109] Higher risk of death was associated with cardiovascular system diseases, immune and metabolic disorders, respiratory diseases, cerebrovascular system diseases, any types of cancer, renal and liver system diseases. Data from a UK cohort has shown that cardiovascular and cerebrovascular disease was significantly more common in patients that had died by 14 days (90% vs 48% in those still alive) and of these congestive cardiac failure was the most notably associated with non-survival (35% vs 11%).[87] Median age in this study was 75 years. Case fatality was 21%; the authors state this was much higher than that reported by other studies of all hospitalised patients; the age of the cohort was also higher. This was also the case at a South West London hospital in which case fatality was 32.6% in a 500 patient cohort; average age was 69 years (SD 19.23, range 1 week to 88 years).[113] It is widely recognised that older age groups have higher rates of underlying comorbidities and both have a correlation with a higher risk of COVID-19 mortality. Among paediatric cases, those with underlying comorbidities are significantly more likely to require hospitalisation and ICU admission and have a higher mortality rate.[103, 114]

Analysis of 53,000 confirmed cases found that 7.7% experienced gastrointestinal symptoms, with approximately 5.7% experiencing diarrhoea.[115] The incidence of diarrhoea is more variable in smaller cohort studies (2-50%).[71, 73, 76, 87, 100, 108, 116-126] [126]Nausea and vomiting are also infrequently reported (5.0% of 1099 confirmed cases from Mainland China).[123, 126, 127] The prevalence of diarrhoea/vomiting in addition to typical symptoms (fever, cough, dyspnoea) was estimated at 5.2% in a large UK cohort of hospitalised cases (n=25,477).[89] Patients reporting with gastrointestinal symptoms were more commonly female, had a longer duration of symptoms before presentation, and had lower 30-day mortality. In one cohort, (n=201) patients with gastrointestinal symptoms were reported as being younger and having less severe disease.[126] A number of early papers cited the need for more research into the possibility of faecal-oral transmission[2, 6, 7, 9-11, 128, 129] following the discovery of viral RNA in the stool samples of COVID-19 patients.[101, 130-135] Early studies reported on single patient cases[130, 131, 133, 136] and/or lacked robust clinical data[130, 132, 137] (i.e. time course of illness, incubation period) which limited interpretation of the epidemiological significance of clinical samples. Pooled detection rates of viral RNA in stool samples have been similar; 43.7% (191/436 cases),[138] 43% (934/2149),[139] and 46.5% (312/671).[140] Evidence has shown that viral RNA can be detected in stool in both children and adults after clearance in respiratory samples,[119, 123, 139, 141-143] in the absence of positive respiratory samples,[144] and following resolution of symptoms.[134, 135, 142, 145, 146] Viral RNA can also be detected in stool in the absence of GI symptoms.[147] The duration of

PCR positivity of stool samples appears to be significantly longer than that of respiratory samples; median 19 days vs. 14 days respectively ($p<0.001$).[148] It is possible that the presence of viral RNA in stool is due to clearance from the mouth/throat into the gastrointestinal tract from swallowing. The transmission risk from non-respiratory samples is still being investigated. Initial attempts at live virus isolation from stool were unsuccessful,[149] however live virus has since been isolated from a stool sample taken approximately 19 days after symptom onset from a severe COVID-19 patient (who subsequently died) in China.[150] Following inoculation of Vero E6 cells, a cytopathic effect was observed after two days, and viral particles with the typical morphology of the SARS-CoV-2 virus was observed. Live virus has also been isolated from 62 stool samples collected from 23 patients using Vero cells; medium duration of shedding was 8 days post symptom onset and the probability of detecting isolated virus dropped below 5% after 15.2 days post symptom onset (95% confidence interval (CI) 13.4 – 17.2).[151] The sample size in this preprint study was very small and further prospective studies that assess time course of viral shedding in stool in relation to illness progression in individual cases is required. Wolfel et al, in the absence of histopathology, analysed the presence of viral sgRNA in clinical samples, which is only transcribed in infected cells and therefore can indicate the presence of actively-infected cells.[149] They reported 'no or only minimal' indication of replication in stool by this method however this was a small study (n=9) and an area of research that requires further work. Limited data from endoscopic examination of infected patients has revealed positive staining of viral host receptor ACE2 in gastrointestinal epithelial cells, leading to the suggestion that gastrointestinal cells are actively infected[135] however this is a single study and an area of research that requires further investigation. To date there is no evidence of direct human-to-human transmission from faecal material.

It is worth noting that the application of standard infection control precautions (SICPs) would prevent ongoing transmission via the faecal-oral route.

Viral RNA has also been detected in blood samples from infected patients.[132, 152-158] However transmission risk via the blood would be expected to be very low and transmission via this route has not been previously reported for respiratory viruses.

A small cohort study describes identification of viral RNA in vaginal swabs in 2/35 women tested, however repeat testing was not conducted and there is the possibility of contamination from the perineum.[159] Two small cohort studies (n=10[160] and n=15[161]) failed to detect any viral RNA in vaginal fluid.[160, 161] Follicular fluid aspirate of a single case was found to be PCR-negative.[162] Viral RNA has not been detected in testicular biopsy samples[163] or expressed prostatic secretion[164] in the small number of those tested although has been detected in semen

both during infection and after symptom resolution.[165, 166] Semen samples from 34 Chinese males taken 1 month after COVID-19 diagnosis were all negative,[167] as was a sample taken 8 days post symptom onset from a single case with mild infection.[92] Semen samples from a cohort of 20 German males including 2 with active infection and 18 in the convalescent phase (8-54 days after absence of symptoms) all tested negative.[168] Samples from 6 males collected 1-3 weeks post symptom onset tested negative in the presence of positive saliva and nasal swabs.[169] Urine samples have tested positive in a small number of cases.[154-156, 166, 170-172] From a meta-analysis of case series and cohorts with a sample size of ≥ 9, the estimated viral shedding frequency in urine was 1.18% (CI 95%:0.14 – 2.87).[173] Viral load in urine was low but detectable and cytopathic effects were observed 3 days after inoculation onto Vero E6 cells[170] but in a separate study, inoculation onto CaCo-2 cells did not yield results.[156] These findings do not indicate infection of the kidneys or bladder however there they do question the possibility of transmission via the urine.

Peritoneal fluid collected during emergency appendicectomy and caesarean section[174] tested negative for viral RNA.[175]

Post-mortem analysis has revealed presence of viral RNA in periodontal tissue.[176]

SARS-CoV-2 has been detected in the tears and conjunctival secretions in COVID-19 patients with conjunctivitis[4, 177-183] and without,[180-182, 184-188] leading to the suggestion that transmission could be possible via the mucous membranes and secretions of the eyes.[189, 190] A positive culture sample grown from an eye swab in Vero E6 cells has been reported.[183] Conversely, a cohort (n=39) that had conjunctival samples consecutively tested reported negative PCR results in all samples.[191] As sampling of the eyes is not routinely carried out, the overall proportion of cases that have positive eye secretions is unknown. A systematic literature review may yield more robust evidence. Presently there is no clear evidence of ocular transmission; further information regarding ocular transmission has been covered in the **eye protection rapid review**. All secretions and excretions from patients with known or suspected COVID-19, should be regarded as potentially infectious.

There is limited evidence regarding mother-to-child transmission. The majority of studies describe development of COVID-19 in the third trimester with subsequent caesarean deliveries and no evidence of vertical transmission.[192 193-213] There is less evidence for vaginal births but the majority have reported no evidence of vertical transmission. [193, 202, 204, 208, 212-228] Seven rapid systematic reviews found no clear evidence of vertical transmission,[217, 229-235] however a systematic review reported a pooled rate of 3.2% (95% CI; 2.2-4.3%) for possible vertical transmission (27/936 neonates tested positive via RT-PCR within 48 hrs of birth).[236] The World

Health Organization in February 2021 provided a definition for determining a confirmed vertical (in-utero) transmission case, requiring a positive neonatal PCR test up to 48hrs post birth as well as a positive sterile sample (e.g. amniotic fluid, neonatal blood) at age <24 hrs.[237] Eight neonates have tested positive by RT-PCT within 24 hrs of birth (2 caesarean, 6 vaginal) with additional positive obstetric tissue samples (amniotic fluid, placenta, umbilical stump); four neonates developed fever at birth, four remained asymptomatic.[238-244] The mother of one of the neonates was symptomatic at delivery but tested negative by RT-PCR, showing positive serology 10 days later.[240] Thirty one reports describe positive neonatal samples in 48 neonates within 36 hrs of birth but obstetric samples were either not collected/tested[245-272] or tested negative.[195, 273-276] In these studies, the majority of neonates (33/48; 2 unreported) were delivered by caesarean section; twenty-nine mothers had mild infection, 2 asymptomatic, 3 severe, and 13 unreported, and all were in the late 2nd or 3rd trimester, bar one who was preterm (29 weeks). A single neonate born at 34 weeks via caesarean section tested positive at 49 hrs of life with positive cord blood and urine but remained asymptomatic.[277] Placental/membrane samples have also tested positive and displayed positive histopathology but in the absence of positive neonatal RT-PCR results.[219, 278-280] Four cases of spontaneous abortion were associated with presence of SARS-CoV-2 in placental tissue following maternal infection in the first[281, 282] and second trimesters.[283, 284] In contrast, this was not the case in a cohort of 24 1st and 2nd trimester spontaneous abortions.[285] Further research is required out-with this rapid review. Antibody testing conducted in neonates has demonstrated mixed results; positive IgM and IgG tests in a number of cases,[286] positive IgG and negative IgM in one case,[287] however in one neonate born to a mother with severe infection, both neonatal IgM and IgG tests were negative.[246] Amongst a cohort of 11 infants born to mothers with COVID-19, all had detectable IgG (100%) and 5 (45.5%) had detectable IgM at birth; RT-PCR test results were all negative.[288] The majority of studies which have tested obstetric samples have not been able to detect viral RNA in amniotic fluid, cord blood, placenta, or breast milk in those tested.[215, 216, 226, 229, 230, 232, 270, 289-294] A systematic literature review (included studies published up to Oct 2020) reported an overall pooled proportion for SARS-CoV-2 RNA detected in breast milk of 2.16% (95%CI: 0.0-8.81%).[295] A small number of cases have reported positive breast milk. RT-PCR testing from a sample taken 1 day after delivery was positive however repeat sampling 2 days later was negative.[296] In a separate case, samples taken 10 days post birth were positive but subsequent tests on days 14-25 were negative.[297] A third case describes positive viral samples from breast milk of an asymptomatic mother, ingested by a neonate that became SARS-CoV-2 positive at 9h hrs post-vaginal delivery, however alternative transmission routes could not be ruled out.[298] Findings from a larger study detected SARS-CoV-2 RNA in the milk samples of 7 (10.6%) out of 66 women with PCR-confirmed infection however viral RNA was not detected via RT-PCR in

subsequent tests on days ranging from 1 to 97 days later.[299] There was no clinical evidence of transmission from these women to their breastfed neonates.[299] One study was unable to detect replication-competent virus in breast milk samples, however these originated from one woman only.[300] Transmission events from breast milk to neonate have not been demonstrated to date.[301-303] The WHO recommend that mothers with suspected or confirmed COVID-19 should be encouraged to initiate or continue to breastfeed.[304] One neonate delivered vaginally in Italy developed symptoms and tested positive 3 days after birth but it is not clear if the baby was isolated from the mother after birth.[305] Whilst many studies describe IPC and isolation measures put in place during and following birth, it is possible that COVID-19 may have been transmitted to neonates from routes other than vertical; immediate testing on delivery may provide more clarity. Overall, evidence suggests very low risk of vertical transmission.

Conclusion:

- The most frequently reported symptoms associated with SARS-CoV-2 infection are cough and fever; anosmia and ageusia (loss of smell and taste) are also frequently reported.
- The incidence of diarrhoea and vomiting during SARS-CoV-2 infection is variable (5-50%).
- The risk of vertical transmission in pregnant women is very low.
- All secretions and excretions from suspected/confirmed infectious individuals should be treated as potentially infectious.

4.3 Atypical presentations

Atypical presentations include cases that do not display the typical clinical symptoms (fever, cough) (which constituted the case definition to date) but may test positive or show radiographic abnormalities (i.e. ground-glass opacity). The absence of respiratory symptoms/fever has frequently been reported in neonates/children[79, 97, 102, 104, 152, 306-309] and less so in adults[72, 120, 310], with diagnosis often relying on RT-PCR and radiological investigation. From analysis of UK cases (n=24,477), those presenting with confusion in the absence of any other symptoms tended to be older (82 years, IQR 75-88).[89] The association between advanced age and confusion was mirrored by a higher prevalence of dementia in these groups. Conjunctivitis in the absence of any other symptoms has also been reported.[179, 311] An atypical presentation occurred in an Italian national evacuated from China and quarantined on arrival with 56 others

as a precautionary measure.[136] This case was a healthy 28 year old male who had no respiratory symptoms but had mild conjunctivitis and slight tonsillar exudate in the presence of positive naso- and oro-pharyngeal samples and stool samples.

A rare Kawasaki-like disease has been identified in a small number of children presenting with COVID-19 in multiple countries.[312-314] Presence of body and acral rashes with or without additional symptoms has been reported.[315] Hormati et al provide a brief report on the admission of two patients to a gastroenterology clinic in Iran with unusual gastrointestinal symptoms; both tested positive for COVID-19 in the absence of respiratory symptoms or fever.[316] Again, no transmission events were reported from these patients. A case report describes possible transmission from a 94 year old patient with atypical presentation (delirium, abdominal pain).[317] Nine HCWs and another inpatient developed COVID-19 after the patient was treated in three wards over 5 days with no infection control precautions, highlighting that there is risk of transmission from atypical presentations where no precautions are taken. From UK data, identification of four symptom patterns (gastro-intestinal symptoms, productive cough, confusion, and pauci-symptomatic presentations) were identified as usefully distinct in terms of clinical utility for identifying atypical presentations.[89] Based on the increasing number of reports of atypical presentation, it may be pragmatic to consider widening the case definition as more evidence arises.

Conclusion:

- Atypical presentations include any symptoms that deviate from, or present in the absence of, the 'classic' range of COVID-19 symptoms and may include the following: conjunctivitis, abdominal pain, confusion and delirium, as well as a rare Kawasaki-like disease in children.

4.4 Asymptomatic transmission

A study by Ma et al (*not peer-reviewed*) that assessed clinical symptoms reported by 7 countries, calculated that, among RT-PCR-positive cases with relevant information (n=329), 49 (15%) were asymptomatic however it was not stated if radiographic symptoms were present.[70] Studies have also reported positive asymptomatic cases, identified during contact tracing, that remained asymptomatic up until the point of negative RT-PCR conversion[318-320] or for the duration of a specified follow-up period.[321-325] Universal screening of 52 asymptomatic obstetric patients in Japan identified low prevalence of infection in the cohort (3.8%); all cases remained asymptomatic.[326] A systematic literature review reported an asymptomatic-positive

prevalence of 20% (95% CI, 17%-25%, n=6,832) with individuals remaining asymptomatic throughout the course of infection.[327] Data suggested that the risk of transmission from asymptomatic individuals may be lower than that of symptomatic individuals, however further research is required. Risk of bias from these studies was high, in part due to selection bias. To date, there has been limited evidence of transmission from positive-asymptomatic cases, however this may be due to the challenge in identifying such index cases. Contact tracing of a Chinese cohort identified 8 clusters with evidence of asymptomatic transmission from 11 asymptomatic infectees.[322] A number of studies report on identification of viral RNA in clinical samples in asymptomatic patients,[145, 152, 321, 328-331] and contact tracing has identified possible transmission from a small number of these cases.[91, 323, 330, 332] Further, saliva samples showed positive replication of viral culture in Vero E6 cells in two asymptomatic/pre-symptomatic individuals.[333] Contact tracing identified a possible asymptomatic index case in a family cluster in China[330] and in Vietnam;[91] both cases had normal CT imaging and no symptoms. Possible asymptomatic transmission was documented on a flight from Italy to South Korea. All passengers were quarantined on arrival at a government facility for 14 days; 6 passengers tested asymptomatic-positive on the first day of quarantine; one passenger developed symptoms on day 8 of quarantine and tested positive, likely having acquired infection from one of the asymptomatic-positive passengers.[323] A systematic literature review that assessed studies up to July 2020 reported a secondary attack rate estimate of 1% (95% CI: 0%-2%) from asymptomatic cases, however the prediction interval ranged from 1-10%.[334] This was in comparison to 6% (95% CI: 5%-8%) for symptomatic index cases.

There may be an association between asymptomatic presentation and younger age.[335] A growing number of paediatric cases have been reported detailing asymptomatic presentations with positive clinical samples however transmission events from these cases could not be proven.[79, 96, 98, 102, 145, 152, 319, 328, 336-338] Assessment of a Korean cohort (n=91) of children <19 yrs old found that 42% were asymptomatic at the time of PCR diagnosis and remained so at follow-up.[339] The proportions of asymptomatic-positive cases are difficult to contextualise due to a lack of point-prevalence-type data from asymptomatic individuals in the wider community. Data from asymptomatic testing of HCWs has revealed a small proportion to be asymptomatic-positive however transmission events from these individuals was not reported. A point prevalence study of US HCWs at a single centre in New York identified 4.1% (4/98) to be asymptomatic-positive at testing, 2 remained asymptomatic at follow-up.[340] A point prevalence study of UK HCWs undertaken in April found that 2.4% (13/545) were asymptomatic-positive at testing and 8 remained so at follow-up.[341] A smaller UK study that routinely tested a cohort of asymptomatic HCWs on a weekly basis identified 44/400 (11%) that tested positive in the

absence of symptoms in the week before or after positivity.[342] Results from the study suggest a likely reflection of general community transmission, however it does raise concern about the risk of transmission from these individuals. Asymptomatic-positive residents have been identified during universal outbreak screening at long term nursing facilities in the US.[343, 344] Up to 10.3% (13/126) were asymptomatic-positive during an outbreak and remained so over a 30 day follow up, but symptom history pre-testing was not obtained.[343] It is essential that follow-up is undertaken to determine if cases remained asymptomatic-positive or were actually pre-symptomatic, and whether any transmission events from these individuals occurred.

Conclusion:

- There is evidence of asymptomatic transmission of COVID-19 however the overall prevalence of this in the population at any one time remains unknown.
- Standard Infection Control Precautions (SICPs) should always be applied in all situations regardless of the infectious nature of the patient.
- All persons should adhere to the requirements for physical distancing and extended use of face coverings whilst in health and care settings.

4.5 Pre-symptomatic transmission

Possible transmission in the incubation period has been reported in a number of studies, mainly small cluster case reports.[329, 345-355] A recent report detailed possible pre-symptomatic transmission in 7 community case clusters in Singapore; date of exposure could be determined in 4 clusters which suggested transmission occurring 1-3 days prior to symptom onset from source patients.[346] Analysis of 72 infector-infectee pairs in South Korea estimated transmission onset to have occurred 0.72 days prior to symptom onset; pre-symptomatic transmission was estimated to be applicable to 37% of cases.[353] Data from a large Chinese cohort (n=1178) estimated infectiousness to have peaked 1.8 days before symptom onset, with the proportion of pre-symptomatic transmission estimated at 62.5% from 43 transmission events recorded in 23 clusters.[322]

Rothe et al report a single case of a Chinese national that travelled to Germany for business and reported hearing coughing from the rows behind on the airplane but was asymptomatic for the duration of contact with German colleagues.[329] Having developed symptoms on return to China, contact tracing was carried out and two German colleagues were identified as positive with mild symptoms. A cluster of cases in Germany developed from this travel-related cluster

and a further pre-symptomatic transmission event was identified between 2 individuals that met in a work canteen; this transmission event was strongly supported by virus sequence analysis.[350]

Contact during the incubation period during a conference was identified as a possible mode of transmission from a single person to 2 family clusters in China; symptoms in the index case developed 2 days after the conference.[347] Transmission in a cluster of young people (16-23 yr olds) in China was linked to an asymptomatic index case who had contact with all persons in the cluster; all cases including the index case subsequently developed symptoms.[348] The estimated incubation period was notably short (median 2 days) in this study. Two further cases of pre-symptomatic transmission were implicated in familial clusters in China; both cases had contact with a pre-symptomatic individual from Wuhan.[347] Contract tracing studies from China have also described possible pre-symptomatic transmission in the incubation period in clusters of community cases.[349, 356] As with the aforementioned studies, there were no severe or critical patients in this cohort. Analysis of an outbreak aboard an aircraft carrier identified 30.5% of those that tested positive to be pre-symptomatic at the time of testing; transmission from these individuals cannot be ruled out due to the close proximity living and working conditions in the cohort.[324]

It is notable that the majority of these studies did not have clinical data available in the incubation period and relied on contact tracing analysis and retrospective data collection, which is prone to recall bias. There is also the possibility of unidentified infectors in these studies. A more robust evidence base is dependent on widespread clinical sampling from mild/community-based cases (and asymptomatic individuals).

Conclusion:

- There is limited evidence of pre-symptomatic transmission of COVID-19 and the overall prevalence of this in the population at any one time remains unknown.
- Standard Infection Control Precautions (SICPs) should always be applied in all situations regardless of the infectious nature of the patient.
- All persons should adhere to the requirements for physical distancing and extended use of face coverings whilst in health and care settings.

4.6 Nosocomial transmission

Data regarding symptoms in HCWs confirms a mirroring of symptoms experienced by the community/general population.[357] In a Dutch cohort of 86 COVID-19-positive HCWs, the majority suffered relatively mild disease and 93% met a case definition of fever and/or coughing and/or shortness of breath.[358] Other symptoms included headache, runny nose, sore throat, chest pain, and diarrhoea. A large proportion (63%) of those screened worked whilst being symptomatic, therefore the possibility of HCW-HCW and HCW-patient transmission (or indeed community transmission) cannot be ruled out, especially considering only 3% reported exposure to a positive inpatient.

There are published reports of clear nosocomial transmission during the earlier stages of the epidemic both in the UK and abroad.[359-361] In Glasgow, nosocomial infection was documented in patients admitted to medicine for the elderly wards across three hospital sites; 103 patients tested positive after 14 days of admission.[361] Mean age of the cohort was 82 years however the infections were recorded prior to the roll out of the Scottish over 70's testing policy (with repeat testing at day 5) on 29th April 2020; had this been in place, infections would very likely have been identified earlier, as atypical presentation and dementia were challenges for diagnosis in this cohort. Reports from a South West London hospital revealed that 51 of 500 analysed admissions developed COVID-19 nosocomially whilst inpatients.[113] A separate inpatient cohort (n=435) from a London teaching hospital reported that 47 cases over a 6 week period met the definition for definite hospital acquisition (symptom onset 14 days or more after admission); many of these cases were identified as having been in the same bay or ward as a patient with PCR-confirmed COVID-19.[362] Analysis of cases admitted between 1st March and 19th April at a south-east London teaching hospital revealed that 7.1% (58 cases) were classed as hospital-associated; median time from admission to symptom onset ranged was 32.5 days (IQR 21-65).[363] Nosocomial transmission from an unknown individual to a patient in an ITU, with subsequent transmission to 5 patients and 16 HCWs within the ward, occurred at a tertiary care university hospital in the UK. The infection cluster occurred after hospital visits were stopped and at the same time as lockdown was announced.[364] A lack of social distancing between staff may have contributed to transmission, as the working environment did not allow adequate spacing; unfortunately WGS was not carried out in this study therefore it was not possible to analyse the transmission events with greater clarity. An outbreak on the paediatric dialysis unit of a German hospital involved transmission from an index patient to 7 HCWs and 3 patients.[365] Transmission from an undiagnosed neurosurgery patient to 12 HCWs occurred at a hospital in Wuhan; appropriate PPE was not worn, with many HCWs not wearing surgical masks.[366]

Possible transmission from an undiagnosed patient to 3 HCWs was suspected to have occurred when performing a bronchoscopy ('procedure' masks were worn, not respirators), however genetic sequencing was not carried out and contact tracing is not described in detail.[367] A case report describes possible transmission from a 94 year old patient with atypical presentation (delirium, abdominal pain) to 9 HCWs and another inpatient after the patient was treated in three wards over 5 days with no infection control precautions.[317] The differing case definitions used by various studies to define hospital-associated COVID-19 make direct comparisons challenging.

Research conducted in March/April 2020 with NHS England Trusts to inform the Scientific Advisory Group for Emergencies (SAGE) suggested that nosocomial transmission of COVID-19 was occurring during that time, with 8.2% of cases being diagnosed 14 days post-admission (inter-quartile range 3.8% to 12.0%). It was reported that few Trusts were assessing the possible involvement of HCWs in transmissions – notably, this was prior to the introduction of universal mask wearing.

As sustained community transmission has occurred as the pandemic has progressed, it has become more challenging to identify true nosocomial transmission events particularly in regards to HCW acquisition. In Scotland, during the period 1st March-6th June, HCWs or their households made up 17.2% (360/2097) of all hospital admissions for COVID-19 in the working age population.[368] Healthcare workers in patient-facing roles were at higher risk of hospital admission (hazard ratio 3.30, 2.13-5.13) than non-patient-facing HCWs, as were their household members (1.79, 1.10-2.91).[368] Most patient facing healthcare workers were in "front door" roles (e.g. paramedics, acute receiving specialties, intensive care, respiratory medicine). Those in non-patient-facing roles had a similar risk of hospital admission as the general population This was not the case in an English cohort; screening of 1654 symptomatic HCWs by an English NHS Trust between March 10-31st identified 240 (14%) positive individuals; comparison of rates between staff in patient-facing and non-patient facing roles found no evidence of a difference, suggesting that data may reflect wider patterns of community transmission rather than nosocomial-only transmission.[369] Mirroring of community transmission was also identified at a large public hospital in Madrid,[370] and at three hospitals in the Netherlands; contacts with COVID-19 individuals was reported from out-with the hospital and from contact with colleagues.[371] Complete genome sequencing of 50 HCW and 18 patients suggested that the observed patterns were most consistent with multiple introductions into the hospital.[371] Genetic sequencing provided confirmatory evidence for community transmission to a HCW, ruling out suspected transmission from two COVID-19 patients.[372] Whole genome sequencing was used as part of outbreak investigations at a hospital in Ireland and revealed

that HCWs moving between wards were responsible for transmission to patients and other HCWs.[373] Transmission between surgical staff at a hospital in Florida, US, was identified prior to the introduction of universal masking in the facility; surgical staff at the time were wearing N95 respirators when treating suspected/confirmed COVID-19 patients; this highlights the risk of transmission potentially not linked to provision of care.[374] Sharing of patient transport was implicated in facilitating patient-patient transmission between renal dialysis patients, where WGS assisted identification of the cluster.[375] Although WGS can help in identifying nosocomial clusters, it is often impossible to determine the source and subsequent direction of transmission.[376] This is especially the case where these is limited data on the genetic background of strains circulating in the community, and incomplete genetic analysis of nosocomial cases. In March 2021, the UK Scientific Advisory Group for Emergencies (SAGE) stated that evidence shows there is variation in both nosocomial infection rates and HCW infection rates, which cannot be explained by levels of respiratory protection alone, with key drivers of nosocomial infection being the community infection rate and hospital occupancy.[377]

Whilst transmission from asymptomatic HCWs has not been documented, a UK study identified a small proportion (0.5% of 1,032) of asymptomatic-positive HCWs during a routine screening study in April 2020, highlighting the risk of transmission from these individuals.[378] HCWs working in 'red' or 'amber' wards were significantly more likely to test positive than those working in 'green' wards (p=0·0042) – this was the case for both symptomatic and asymptomatic-positive HCWs. Contact tracing at a hospital in the US that involved testing of asymptomatic HCWs revealed a number of exposures between staff to have occurred when the index HCW case was pre-symptomatic.[379] None of the confirmed HCW cases occurred in staff working on COVID-19 designated wards; exposure on non-COVID-19 wards was attributable to delayed diagnosis which was reduced as availability of testing and awareness of atypical presentations increased, and as routine admission screening was implemented. The authors proposed that some of the transmission to HCWs might have been attributable to non-compliance with facemask use in nonclinical shared work areas (e.g. nursing station, staff work, or break rooms) or during activities such as meals when facemasks were removed, and social distancing was not maintained. Data from 4 London care homes identified 44 residents (17% of the 264 cohort) that were asymptomatic-positive and remained so at follow-up.[105] Further, 7.9% were pre-symptomatic.[380] Some SARS-CoV-2 sequence variants were highly similar between residents and/or staff within a single care home; there were also multiple distinct clusters of SARS-CoV-2 sequence types within single nursing homes, suggestive of multiple introductions.[105] Analysis of 24 Irish care homes found the median proportion of asymptomatic-positive staff was 19.6% (IQR 11.8-52.3%); asymptomatic was defined as without symptoms

7-days either side of a test.[381] Over 25% of residents with lab-confirmed infection were asymptomatic. It was not possible to determine the impact of these individuals on transmission in these settings.

In Scottish acute settings, unpublished outbreak reporting has highlighted the contribution of both HCWs and patients to nosocomial transmission (and visitors to a lesser degree). A number of recurring themes have emerged when considering factors likely to contribute to transmission. Non-clinical HCW activities include car-sharing, socialising outside of work, and shared break times. Patient risk was linked to inpatients not wearing face coverings, patients moving around clinical areas, and patients being transferred between wards prior to a PCR result. Poor compliance with mask wearing (in HCWs and visitors) and physical distancing as well as HCWs working whilst symptomatic were also identified. A report published by the Healthcare Safety Investigation Branch concluded that more should be done with regards to the design of ward work systems and equipment layout to mitigate the risk of nosocomial transmission.[382] In particular, the investigation observed limited mitigation strategies in the design of the physical environment, and in staff work patterns, to enable staff to take breaks in environments whilst maintaining physical distancing. Typically, due to limited time available to take a break, staff would need to use small rooms adjacent to their clinical environment, with a lack of opportunities to increase levels of ventilation. Although the investigation involved NHS England trusts, there are similarities in the built environment and nursing cultures in Scotland, and these issues are likely experienced in other countries too. At a German hospital, removal of masks during staff breaks was identified as a potential contributor to transmission between staff,[383] this was also noted as a risk factor in an Indian cohort.[384] In a French HCW cohort (n=99), not wearing facemasks during staff meetings was associated with risk of infection.[385] Expert opinion has also identified the difficulties in maintaining adherence to physical distancing, particularly in older builds with nightingale wards, highlighting that a whole systems approach should be implemented to mitigate human nature/behaviour and support adherence.[386] Looking at non-acute settings, a study of Canadian care homes indicated that overcrowding was associated with higher incidence of infection and mortality, indicating that inability to isolate residents may have facilitated transmission.[387]

With regards to the risk of transmission from visitors, there is a lack of clear evidence in the literature. Visitors have been implicated as potential sources of transmission in Scottish acute settings in a small number of incidents (unpublished) however the nature of retrospective investigation coupled with the complexities of contact tracing during a global pandemic prevents confirmation of the precise transmission routes. Visitors are also at risk of acquiring COVID-19 whilst visiting healthcare facilitates and anecdotally this has occurred in Scotland. Whilst the

aim from an infection prevention and control perspective is to reduce the infection risk, consideration must be given to the unintended negative effects on patients and families where visiting is restricted. This is particularly an issue in situations involving critical care and end of life care. The Scottish Government has produced guidance to support the safe reintroduction of visitors into hospital settings,[388] the specifics regarding requirements for visitors is outlined in the NIPCM COVID-19 addendum.[389]

It is notable that not all unprotected exposures to COVID-19-positive individuals result in transmission, even when being exposed to AGPs without respiratory protection.[59] None of the 21 HCWs that reported contact with an undiagnosed patient with mild respiratory symptoms at a Swiss hospital tested positive when tested 7 days later.[390] The patient underwent routine clinical examinations, blood draws, electrocardiograms, chest X-rays and had nasopharyngeal swabs taken; masks were never worn by HCWs during the patient's care. In Germany, a physician worked over a number of days in a hospital whilst symptomatic (coughing, fever) and with no mask, but did not transmit infection to any of the 254 identified contacts (HCWs and patients).[391] In Singapore, 41 HCWs were exposed to multiple AGPs at a distance of less than 2 metres for at least 10 minutes while wearing predominantly surgical masks (only 25% wore N95 respirators) whilst caring for a patient with undiagnosed COVID-19; none of the HCWs developed symptoms or tested positive (with repeat testing) in the 14 days following exposure.[392] Exposure to 5 patients with atypical presentations at a hospital in Singapore was not associated with subsequent infection in HCWs; the majority were wearing surgical masks at the time; the potential impact of varying viral load in these patients was not investigated.[393] This highlights the role of multiple factors in transmission.

Conclusion:

- Standard Infection Control Precautions (SICPs) should always be applied in all situations regardless of the infectious nature of the patient.
- Droplet precautions should be implemented when in close contact (within 2 metres), or providing direct patient care to a suspected/confirmed COVID-19 patient.
- Airborne precautions should be implemented when undertaking an AGP on a suspected/confirmed COVID-19 patient within the medium risk (amber) and high risk (red) pathways.
- Visitors should be managed according to the NIPCM COVID-19 addendum.

- When not providing patient care, HCWs should continue to adhere to the pandemic controls (physical distancing, extended mask wearing) as outlined in the NIPCM COVID-19 addendums.

4.7 Reinfection

There have been a small number of published articles detailing individuals (n=13) having two distinct COVID-19 illnesses caused by genetically distinct SARS-CoV-2 strains.[394-403] Two of these cases were asymptomatic in both episodes of infection.[399] One case was re-infected with the new UK strain VOC-202012/01 of lineage B.1.1.7.[400] The time period from PCR-positivity in the first to the second infection episode ranged from 48 days to ~8 months. None of these cases were associated with onward transmission. The UK SIREN study reported 47 cases of potential reinfection in HCWs based on an initial PCR positive test followed by a subsequent PCR positive test a minimum of 90 days later; however, genomic analysis was not undertaken to confirm whether the infections were genetically distinct.[404] The median interval between the first PCR positive date and the potential reinfection PCR positive date was 162 days (95-223). Details regarding symptoms related to the second PCR test were not provided. There is so far nothing to indicate that a change in IPC measures is required to manage these types of cases. The ECDC recommend that a case definition for reinfection should include laboratory confirmation of two infections by two different strains but that the minimum genetic distance and the minimum time period between illnesses is still to be determined/supported by phylogenetic and epidemiological data.[405] In a technical report published 8 April 2021, the ECDC[406] proposed a standardised surveillance case definition for suspected SARS-CoV-2 reinfection taking into account the emerging variants of concerns (VOCs) with immune escape potential. A *suspected* COVID-19 reinfection case is defined as: “Positive PCR or rapid antigen test (RAT) sample ≥ 60 days following: a previous positive PCR; previous positive RAT; and previous positive serology (anti-spike IgG Ab)”.[406] The Pan American Health Organization in collaboration with the WHO advise that a confirmed case should be determined by complete genomic sequencing for both the primary infection sample and secondary infection sample to confirm they belong to different genetic clades or lineages, regardless of the number of single nucleotide variations (SNV), stating that the virus is expected to mutate by approximately two SNVs per month.[407]

In regards to routine testing of recovered healthcare workers, Scottish guidance advises that social, community and residential care staff who have previously tested positive by PCR are exempt from being retested for a period of 90 days from their initial illness onset, unless they develop new symptoms.[408] This is to account for possible prolonged shedding and based on the

assumption of immunity in the immediate term following infection. Scottish Government guidance for acute care staff (those working in oncology, elderly care and mental health wards, with stays over three months) states that a return to weekly PCR testing is not recommended following a positive result, only if symptoms reappear should staff be tested again, however do not advise when PCR testing should recommence.[409] However, it is advised that staff who tested positive from a PCR test are exempt from commencing/recommencing *lateral flow testing* for a period of 90 days after their PCR positive test was taken. Voluntary twice-weekly lateral flow testing for asymptomatic HCWs was introduced in December 2020.[410] From the reinfection cases identified to date, it would appear that immunity is either not induced and/or not protective against different strains; follow-up and analysis of larger COVID-19 cohorts (and ideally asymptomatic healthcare worker testing cohorts) will provide valuable information on this topic. The ECDC report there are no studies designed to assess risk of transmission from reinfection, but that cohort studies to date estimate some protective effect up to five to seven months, which is lower in individuals aged 65 years and older, and does not apply to emergence of variants of concern.[411]

Conclusion:

- All persons, including those who have recovered from COVID-19 infection, should continue adhering to the IPC measures currently in place to mitigate the risk of COVID-19 transmission.

4.8 Incubation period

Many of the studies published to date are limited by small sample sizes and over-representation of severe cases, the incubation period for which may differ from that of mild cases. Evidence suggests an incubation period of 5-6 days[7, 10, 80, 108, 122, 350, 354, 357, 412-431] with a range of 1-14 days[7, 8, 11, 73, 76, 108, 127, 353, 357, 415, 416, 418, 419, 429, 432-436] from infection to symptoms surfacing. Further analysis of 2,555 Chinese community cases indicates a longer incubation period of 9 days.[437] Lauer et al estimate that most (97%) of those who develop symptoms do so within 11.5 days of infection (95% CI, 8.2-15.6).[414] Analysis of a small Chinese cohort (n=183) provided an estimate that 95% of those who develop symptoms will do so within 14 days of infection (95% CI; 12.2-15.9).[438] Consequently only a limited number of cases will potentially develop symptoms out-with the 14 days of self-isolation that is required following contact with a confirmed case. A change to the isolation period required for contacts from 14 to 10 days was announced by the UK Chief Medical Officers' which came into effect from 14th December

2020.[439] Analysis of viral load in a Spanish cohort found that time to symptom onset decreased in a dose-dependent manner as viral load at baseline increased.[440]

Conclusion:

- The incubation period for most individuals is reported as 5-6 days (range 1-14 days).
- Self-isolation for 10 days is recommended for contacts of symptomatic cases.

4.9 Infectious period

In most cases, individuals are usually considered infectious whilst they have respiratory symptoms; how infectious an individual is likely depends on the severity of their symptoms and stage of their illness. Initial data from Wuhan suggested a median time from symptom onset to clinical recovery for mild cases of approximately 2 weeks, and 3-6 weeks for severe or critical cases however this data is likely biased by the fact that the majority of cases included in the study were hospitalised; the proportion of milder community cases is likely underestimated.[415]

Less is known about the duration of infectivity. From limited international data, the balance of evidence is that, for mild cases of infection, infectivity (as determined by respiratory RT-PCR sampling) peaks at symptom onset and significantly reduces 7 days after the onset of symptoms but appears to take longer for severe cases.[149, 415, 441-446] Community transmission on the day of symptom onset (when symptoms are mild and non-specific) has been reported but is reliant on retrospective self-reported data.[447] Analysis of 301 hospitalised cases revealed that the positive rate of RT-PCR assay was highest at day 0−7 (97.9 %) after symptom onset then decreased with time; after 4 weeks, 26.3% of samples were still positive.[448] It was also observed that patients ≥65 years old shed virus for a longer period (22 days vs 19 days, p=0.015). A further cohort (n=1023) of mainly hospitalised patients demonstrated the positive rate of RT-PCR in nasopharyngeal samples to be highest (89% (95% CI 83-93) between 0 and 4 days post-symptom onset, dropping to 54% after 10-14 days.[449] Limited data in children has shown viral load peaking at day 2-3 after symptom onset.[450] Overall, the evidence base suggests that viral load likely peaks at or immediately following symptom onset.

Prolonged detection of viral RNA in respiratory and stool samples for up to 28 days (and in some cases up to several months) after symptom onset has been reported from hospitalised and community cohorts.[94, 450-463] Being immunocompromised may also be associated with prolonged PCR detection.[464-467] Analysis of a US cohort of 121 patients and HCWs demonstrated an average time of 24 days after symptom onset for transition from RT-PCR

positive to negative; 10% remained positive 33 days after symptom onset.[468] Details of symptoms and infection severity were not reported, however there is evidence that patients with severe infection (requiring ICU admission) shed virus (as detected in nasal swabs) for significantly longer than non-ICU patients.[185, 445, 446, 459] In one cohort study (n=76, 30 severe, 46 mild), 90% of mild cases were PCR-negative by 10 day post-onset, while all the severe cases were still positive at 10 days post-onset.[445] In an Italian community cohort, viral clearance was achieved by 60.6% (704/1162) of patients, with a median of 30 days from diagnosis (IQR 23-40) and 36 days from symptom onset (IQR 28-45).[469] From a retrospective cohort of 537 symptomatic community cases in Germany (isolating at home), 53.5% remained positive by PCR at 14 days after symptom onset.[470] A mean duration of viral RNA detection was estimated at 14.96 days after symptom onset. Hospitalisation before home isolation was associated with a 26% longer duration of PCR positivity compared with patients in home isolation throughout (time ratio: 1.26; p=0.049). Details regarding the presence and severity of symptoms throughout the isolation period were not provided. In a small retrospective cohort of patients (n = 206) admitted to hospital with mild disease (i.e. no fever, respiratory distress and sufficient blood oxygen), mean interval between symptom onset and viral clearance was 38.1 days (SD 8.7; range 15 – 62) and was significantly longer amongst patients with digestive symptoms (40.9 days), or both digestive and respiratory symptoms (42.0 days), $p < 0.001$.[471] A meta-analysis conducted to assess viral shedding time (VST) reported the pooled mean VST from 35 included articles was 16.8 days (95% CI 14.8-19.4), with significantly longer VST in patients with symptomatic infection compared to asymptomatic patients (19.7 days, 95% CI 17.2-22.7 vs 10.9 days, 95% CI 8.3-14.3; $p<0.05$). Additionally, longer VST was observed for adults, and those with chronic disease. Viral shedding lasted significantly longer in stool samples than in respiratory samples (30.3 days, 95% CI 23.1-39.2, vs 17.5 days, 95% CI 14.9-20.6; $p<0.05$).[472]

Prolonged viral RNA detection is an issue where discharge/release from isolation is reliant on 2 consecutive negative PCR results. Analysis of a small cohort of cases in Wuhan that returned home after a 14 day isolation period following hospitalisation and were still PCR-positive found no onward transmission to household contacts.[473] None of the household contacts developed any symptoms and both PCR and IgM/IgG antibody testing were negative. Median time of PCR-positivity was 78 days (IQR 67.7-84.5) with the longest duration found to be 120 days. A larger Wuhan cohort (n=2,466) that had a repeat positive PCR test following discharge from hospital had 4,079 close contacts – none of the close contacts had a positive PCR result, suggesting the risk of transmission from prolonged shedders may be small.[474] Discharge was dependent on 2 negative PCR tests taken 24 hrs apart; this implies that either false-negatives

were occurring or that shedding fluctuated over time. In a separate study, exhaled breath condensate samples collected ~40 days post-symptom onset from 2 elderly hospitalised patients (medium/severe disease) that met the requirements for discharge (negative PCR throat swab and clinically well) tested positive however these samples were not cultured to test viability.[475] Repeat testing with a larger sample size would provide a more reliable evidence base regarding exhaled breath condensate sampling.

Prolonged viral shedding may not correlate with infectiousness; there is limited evidence regarding this as the infectious dose required for transmission has yet to be determined. Wolfel et al assessed 9 cases in Munich, Germany and found that live virus could be isolated from respiratory samples taken within the first 7 days of symptoms but not from day 8 onwards, *even though viral RNA could still be detected in samples*.[149] Live virus isolation may also be dependent on viral load; samples containing under 10^6 copies/mL (or copies per sample) never yielded an isolate.[149] In the absence of histopathology, the same study analysed the presence of viral sgRNA which is only transcribed in infected cells and therefore can indicate the presence of actively-infected cells in samples. Throat swabs taken up to day 5 were positive while no sgRNA was detected thereafter. This suggests that as viral load reduces in the later stages of infection, so too does transmission risk. This was demonstrated in a US cohort of HCWs in which viral load peaked in the first few days after symptom onset then became negatively associated with days since symptom onset, reducing significantly by day 10.[476] Wolfel et al estimate that, for patients beyond day 10 of symptoms and with less than 100,000 viral RNA copies per ml of sputum, early discharge with ensuing home isolation might be appropriate.[149] Analysis of sgRNA in samples from a patient cohort (n=35) with mild infection found it was detectable in 18/22 (81.8%) of specimens collected <8 days after symptom onset but only in 1/11 (9.1%) of those collected >9 days after symptom onset (P=0.0003).[477] The median viral load in culture-positive samples was significantly higher than in culture-negative samples (p=0.00001). Analysis of 754 samples from 425 symptomatic cases in the UK found that levels of viral RNA (determined from the RT-PCR cycle threshold values) in the upper respiratory tract were greatest around symptom onset, steadily decreased during the first 10 days after symptom onset and then plateaued.[478] Detection of culturable virus peaked around the time of symptom onset; median duration of virus shedding as measured by culture was 4 days (IQR 1-8, range -13 to 12). Culture positivity rate was significantly higher during week 1 than week 2 (74% vs 20%, p=0.002). Ten days after symptom onset, the probability of culturing virus declined to 6.0% (95% CI: 0.9–31.2%). A Canadian study found there was no growth on viral culture from samples taken >8 days since symptom onset; the probability of obtaining a positive viral culture peaked on day 3 and decreased from that point.[479] Vero cell

infectivity was only observed for samples with a cycle threshold value <24. A further study that conducted viral culture of 46 cases reported a mean duration from symptom onset to culture positivity of 4.5 days (range 0-18 days); whilst one patient continued to be culture positive to day 18, no others were positive beyond 10 days after symptom onset.[480] Cultures were significantly more likely to be positive from samples collected within the first week after symptom onset when compared to the second week (80% vs 45%, p=0·002), and from samples collected in the second week compared to the third week (45% vs 4%, p<0·001). Ten days was also reported as the maximum number of days post-symptom onset that viral culture could be demonstrated in positive samples from outpatients with mild infection; samples from moderate to severe hospitalized cases could be cultured up to 32 days post-symptom onset.[481] Prolonged viral culture of up to 22 days following the first positive PCR result has been reported elsewhere and was found to be associated with persistence of symptoms.[482] Viral culture has also been demonstrated in children during early acute illness.[483] A French study that assessed viral culture (n=124 samples) in relation to viral load of PCR clinical samples demonstrated a significant correlation between successful isolation of virus in cell culture and Ct values of 13-17.[484] Culture positive rate then decreased progressively according to Ct values to reach 12% at 33 Ct; no culture was obtained from samples with Ct>34. These findings are similar to those reported elsewhere; the median Ct value associated with recoverable virus in a US hospitalised cohort (n=29) was 18.17 which was significantly lower than the median Ct value that did not correlate with infectious virus recovery (27.5, P<0.0001). Samples with a Ct value below 23 yielded 91.5% virus isolates.[482] Taiwanese data also indicates that samples with Ct values of >32 did not yield culturable virus.[485] Similarly, in a hospitalised Singapore cohort (n=100, 20% required supplemental oxygen),[486] and in an Italian hospitalised cohort (n=83, ~15% supplemental oxygen),[487] no virus was able to be isolated when the Ct value was >30, or when patients were >14 days post symptom onset (or 3 days post symptom resolution). In a small hospitalised cohort (n = 174) in Spain, viable SARS-CoV-2 was detected in samples with high viral load (Ct ≤ 25) in cases with both mild or severe symptoms. Moreover, viable virus was detected in a small proportion (5% of mild cases and 15% of severe cases) of respiratory samples with low viral load (Ct ≥ 35).[463] It has been proposed that each centre should perform its own correlation study to aid with determination of infectivity cut-off, which may be used to assist decision making regarding hospital discharge.[484] However, UK guidance (published 28th October 2020) advises that a single Ct value in the absence of clinical context cannot be relied upon for decision making about a person's infectivity.[488] One study, in contrast to the evidence base described, has demonstrated prolonged infectivity as measured by culture on Vero E6 cells of 73 and 102 days (ct values 26.21 and 27.15 respectively); both cases were elderly and had mild symptoms.[489] Further research is required to determine if these cases are outliers. In

summary, the evidence base suggests that culture-positive samples tend to have higher viral loads than culture-negative samples, culture positivity peaks close to symptom onset, and culture positivity (and viral load) significantly decreases ~10 days post symptom onset. The impact of these findings on transmission risk is of obvious interest. Analysis of 282 mild transmission clusters in Spain observed an increased secondary attack rate (24% vs 12%) when the baseline viral load of the index case was 1×10^{10} copies per mL or higher (adjusted odds ratio per log10 increase in viral load 1·3, 95% CI: 1·1–1·5).[440] Further research is required in the area of viral isolation and cycle threshold analysis to develop a robust evidence base to assist with discharge decision-making.

Data from a number of studies has demonstrated a pattern with viral clearance with regard to clinical sample type; viral presence in respiratory samples appears to peak in the earlier stages of infection then decreases with time whilst the opposite has been observed with stool samples.[134, 135, 143, 145, 155, 457] Analysis of hospitalized cases in China indicated an association between hypertension and delayed viral clearance.[442, 490] Hypertension is the most frequently reported CV comorbidity associated with COVID-19 infection; hypertensive patients also have a higher mortality rate compared to normotensive patients.[106] This has led to the suggestion that treatment with ACE2 inhibitors (antihypertensive medication) in patients with hypertension might facilitate SARS-CoV-2 to enter the targeted cells via ACE2 receptors in the respiratory system, and thus prolong the time of viral clearance.[442] Further research is required to detangle the association between severe disease, comorbidities, and delayed viral clearance.

Reports that suggest possible infectivity in the asymptomatic period are based on limited evidence from largely retrospective observations during contact tracing, and identification of viral RNA in clinical samples post symptom resolution.[10, 134, 152, 328, 329, 432, 491-493]

Concerns over risk of transmission in the incubation period have been raised following identification of possible transmission events in the incubation period from contact tracing studies, and observations of positive clinical samples prior to symptom onset. A report from a long term care facility in which two rounds of 'point prevalence' COVID-19 screening were carried out (1 week apart), found that more than half the residents (27 of 48) who had positive tests were asymptomatic at testing.[494] Further,17 of 24 specimens (71%) from pre-symptomatic persons (those who were asymptomatic at testing but went onto develop disease) had viable virus by culture 1 to 6 days before the development of symptoms. Possible transmission events from these individuals were not reported. Identification of RT-PCR positivity in the incubation period has also been reported in South Korea; 41 out of 213 tested (19.2%) were asymptomatic at testing.[495] Progression to disease was not reported; all individuals were isolated therefore

transmission events in this cohort were not assessed. Pre-symptomatic infection with cytopathic effort observed on cell culture was reported from a case in Sweden, which infers infectivity in the pre-symptomatic period.[496] Unfortunately, contact tracing studies frequently lack accompanying clinical data i.e. RT-PCR testing from the incubation period, due to their retrospective nature.

Knowledge is also limited regarding the transmission dynamics of asymptomatic-positive cases. A progressive decline in viral load from day of detection to day of last positivity is a similar pattern to that seen in symptomatic positive cases.[497] Analysis of the initial RNA load and threshold cycle value ('Ct' value, which is inversely proportional to the viral load) from a number of small studies indicates a lower viral load in asymptomatic cases during hospitalisation.[155, 331, 365, 450, 498] In one study, symptomatic cases had an approximately 200-fold higher viral load.[365] However, a larger study found that the initial threshold cycle value of nasopharyngeal RNA in asymptomatic carriers was similar to that in pre-symptomatic and symptomatic patients, but that viral clearance was faster, as the RNA negative-conversion occurred earlier for asymptomatic cases.[336] From this, the authors deduced that the communicable period of asymptomatic cases was shorter than pre-symptomatic patients (9.63 days vs.13.6 days). Significantly faster viral clearance in asymptomatic cases has been demonstrated in a number of small studies.[91, 331] Analysis of 82 Chinese cases found that those with respiratory symptoms (cough) had a statistically significantly longer duration of positive testing by nasopharyngeal swab compared to patients presenting without respiratory symptoms (17 days vs. 13 days, $p = 0.041$).[499]

In general, the evidence regarding the transmission dynamics from asymptomatic cases is weak; further research is required.

Guidance from the ECDC recommends that COVID-19 patients may be discharged from hospital based on: a) clinical resolution of symptoms, and b) evidence for viral RNA clearance which would be 2 negative RT-PCR tests from respiratory specimens at 24 hrs interval at least 8 days after onset of symptoms, where testing capacity permits.[500] However in light of the widespread community transmission, clinical criteria should gain priority. This is consistent with Scottish and UK guidance which recommends discharge as soon as the patient is clinical well enough (i.e. symptoms may still be present).[501, 502] Those discharged should self-isolate for 14 days (minimum) from symptom onset (or first positive test if symptoms onset undetermined), with absence of fever for 48 hours without the use of antipyretics.[501, 502] Asymptomatic individuals who test positive for SARS-CoV-2 through routine PCR testing on admission to hospital for non-COVID-19 reasons, can be advised on discharge to self-isolate for 10 days from their positive PCR test, and to isolate for a further 10 days, if the individual goes on to

develop COVID-19 symptoms.[502] However, patients being discharged into a care facility (residential or care home) should have 2 negative tests prior to discharge, unless there are overriding clinical reasons where this is not appropriate (patient doesn't consent or it would cause distress).[501] A 14-day isolation period is required for asymptomatic patients discharged to a care facility.[502]

Conclusion:

- Transmission is most likely to occur whilst an individual is symptomatic.
- In mild cases of infection, where hospitalisation is not required, the risk of transmission is thought to significantly reduce after 7 days.
- Individuals with symptoms consistent with COVID-19 should self-isolate for 10 days from symptom onset.
- In severe cases the risk of transmission may extend beyond 7 days therefore Transmission Based Precautions (TBPs) should remain in place for the duration of hospital admission or home isolation until cessation of symptoms.
- In hospital settings clinicians should consider extending isolation for some cases e.g. elderly, immunosuppressed, if they remain symptomatic after 14 days until test results are available.
- Patients discharged from hospital should self-isolate for 14 days from symptom onset (or first positive test if symptom onset undetermined) with absence of fever (without use of antipyretics) for 48 hours.

5. Personal protective equipment

5.1 Surgical face masks

It is vital that a distinction is made between the evidence pertaining to fluid-resistant surgical face masks (FRSM) (Type IIR) and standard (non-fluid-resistant) surgical face masks (Types I & II). Surgical masks are tested against the safety standard BS EN 14683:2019; this series of tests measures the performance of a surgical mask in bacterial filtration efficiency (BFE), breathing resistance and splash resistance. Type II and Type IIR surgical masks are both

tested against this standard with them needing to meet a minimum BFE of 98%; however only Type IIR masks must pass the splash resistance test with a resistance of at least 16.0kPa. The terms 'fluid resistant' and 'fluid repellent' are often used interchangeably to denote a Type IIR surgical mask, however, terminology may vary internationally and a 'fluid repellent' mask may occasionally describe a mask that does not meet the BS EN 14683:2019 splash resistance standard and which is not suitable for protection against splash or spray i.e. a Type II surgical mask. In the UK, when recommended for infection prevention and control purposes a 'surgical mask' will be a fluid-resistant (Type IIR) surgical mask.

Standard surgical face masks (i.e. Type II) can be worn by an infectious individual to prevent transmission.[503-505] To demonstrate this, a study by *Leung et al* tested the efficacy of surgical masks at reducing the detection of seasonal (non-COVID-19) coronavirus in exhaled breath from infected patients.[506] Coronavirus could be detected in ~40% of samples collected from non-mask wearers (n=10) but was not detected in exhaled air from patients that wore surgical masks (n=11). The masks used were Type II, i.e. they were not fluid-resistant. This study was limited by the small sample size – due in part to the fact that a large proportion of infected participants had undetectable viral shedding in exhaled breath. Studies assessing Type II surgical masks have also reported reduced detection of seasonal influenza in exhaled breath in mask wearers.[506, 507] An environmental sampling study of multiple sites (prior to environmental cleaning) surrounding 3 hospitalised COVID-19 patients yielded negative results; two of these patients wore surgical masks continually and the critical bed-bound ICU patient had a closed loop circuit ventilator.[508] All patients tested positive by throat swab on the day of sampling and the masks and the closed suction tube tested positive.

Whereas standard surgical face masks can be worn by an infectious individual to prevent transmission, it is the fluid-resistant nature of FRSMs that provides additional protection to the wearer (e.g. HCW) against droplet-transmitted infectious agents. Guidance consistently recommends that HCWs should wear a Type IIR FRSM as PPE when caring for a patient known, or suspected, to be infected with an infectious agent spread by the droplet route.[60, 503, 505, 509-513] In UK health and care settings, surgical masks must be fluid-resistant, 'CE' marked and compliant with Medical Device Directive (MDD/93/42/EEC) and the Personal Protective Equipment Regulations 2002.[514-519]

Surgical masks do not provide protection against airborne particles and are not classified as respiratory protective devices.[520] Assessment of PPE use against similar coronaviruses i.e. severe acute respiratory virus (SARS), provides weak evidence that droplet precautions (i.e. surgical masks) are adequate. A systematic review and meta-analysis combining

6 case-control and 3 cohort studies, found that use of respirators/masks provided significant protection against SARS-CoV among exposed HCWs (OR=0.22; 95% CI: 0.12-0.40). Wearing surgical masks (OR=0.13; 95% CI: 0.03-0.62) or N95 respirators (OR=0.12; 95% CI: 0.06-0.26) (versus no RPE) both reduced the risk of SARS-CoV by approximately 80%. No protective effect was reported for disposable cotton or paper masks. The existing evidence base in the review was sparse and the indications (and compliance) for mask/respirator use varied between the included studies.[521] The type of surgical mask was not reported in all studies. A case control study that compared PPE use in 241 non-infected HCWs and 13 infected HCWs with documented exposure to 11 index patients with SARS-CoV found that none of the infected staff wore surgical masks or respirators (2 wore paper masks). [522] However, RT-PCR analysis was not used to confirm infection in this study (confirmation of HCWs relied on serological analysis), and recall bias for PPE use may have affected results. Inadequate reporting of RPE/mask indications and compliance was a major limitation in a recent systematic review and meta-analysis conducted by *Bartoszko et al*, which included 4 RCTs and reported that, compared to N95 respirators, the use of medical masks was not associated with an increase in laboratory-confirmed viral respiratory infection or respiratory illness.[523] There was significant variation in surgical mask type between the included studies (Type IIR FRSMs were not used in every study). A rapid review conducted specifically to assess the RPE requirements for COVID-19 in primary care determined that the evidence base was weak as the included studies were focussed on influenza transmission, not COVID-19; these studies provided weak support for the use of standard surgical masks in non-AGP settings.[524] A recent update to a Cochrane systematic review that assessed full body PPE for the prevention of exposure to highly infectious diseases (including COVID-19) found that covering more parts of the body leads to better protection but usually comes at the cost of more difficult donning or doffing and less user comfort, and may therefore even lead to more contamination.[525] Certainty of the evidence was judged as low due to the fact that almost all findings were based on one or at most two small simulation studies.

For all non-AGP scenarios, there is no clear evidence that respirators offer any additional protection against coronaviruses. The UK Health and Safety Executive (HSE) position regarding RPE has remained unchanged; currently the use of respirators, such as FFP2 or FFP3, are only for the highest risk aerosol generating procedures which are undertaken in medical settings and during dental procedures (*correspondence provided by the UK IPC Cell*). The UK Scientific Advisory Group for Emergencies (SAGE) acknowledged that the impact of greater use of FFP3 masks on the overall level of transmission in HCWs is unknown, but that

this should not be taken to show an absence of effect, stating that policy-makers may have to make decisions based on a range of additional factors.[377]

The World Health Organization, Canadian Government guidance, and Australian Government guidance recommends surgical face masks for routine care (non-AGP) of suspected/confirmed COVID-19 patients.[526-529] The US Centers for Disease Control and Prevention (CDC) recommend that HCWs can wear a well-fitting facemask for protection during non-AGP patient care encounters with patients not suspected of having COVID-19 (respirators are optional).[530] This would equate to care for patients on the low risk (green) pathway in the UK.

In the 6th update of ECDC IPC guidance, respirators rather than surgical masks are recommended when caring for suspected/confirmed patients.[18] The ECDC make reference to the weak evidence base underpinning their recommendation, stating that "*with the exception of AGPs, it is unclear whether respirators provide better protection than medical masks against other coronaviruses and respiratory viruses such as influenza*".[18]

In regards to source control, an experimental study using 12 healthy volunteers found that air escape from the sides/top of a 3-layer pleated surgical mask led to a reduction in efficiency from >90% (for air that passes through the mask) to ~70% while talking and a reduction from 94% to 90% for coughing.[531] This demonstrated that whilst air escape does limit the overall efficiency of surgical masks at reducing expiratory particle emissions, masks do provide substantial reduction. Using healthy volunteers in an experimental set up, a fluid resistant surgical mask was found to significantly reduce aerosol emissions from both speaking (0.113 vs 0.038, $p = 0.002$), and coughing (1.40 vs 0.075, $p < 0.001$).[64] An experimental study using simulated SARS-CoV-2 virus expulsions and mannequin heads demonstrated a synergistic protective effect when both the spreader and receiver wore a mask (cotton or surgical), suggesting that universal face covering/mask wearing is likely to have a protective effect overall.[532]

Guidance issued by the Scottish Government on 23rd June advised that all staff in hospitals and care homes in Scotland are required to wear a 'medical' face mask at all times throughout their shift, from 29th June onwards.[533] Patients and visitors to hospitals and care homes must wear a face covering. Staff must also wear a face covering when they are out with clinical areas/not on duty. Face mask/covering requirements were extended to include primary care (GP practices, dentists, opticians and pharmacies) and wider community care (including adult social or community care and adult residential settings, care home settings and domiciliary care) on 18th September.[533] The main purpose of these measures is to prevent transmission of the virus from the person wearing the face mask, in recognition of the risk of pre-symptomatic and asymptomatic transmission, and the difficulties in maintaining physical distancing in the

workplace. These recommendations are in-line with guidance produced by the World Health Organization, which states that in areas of known/suspected community or cluster transmission, universal masking should be implemented for all persons (staff, patients, visitors, service providers, others) within the health facility.[20] This was based on expert opinion.

The new Scottish COVID-19 addendum for acute care settings published within the NIPCM on October 27th 2020 states that HCWs should wear a type IIR fluid resistant surgical mask for all direct contact with patients, and when carrying out AGPs in the green pathway.[389] Inpatients across all pathways must wear a surgical facemask at all times if it can be tolerated and if it does not compromise their clinical care.

Conclusion:

- Health and care workers across all pathways should wear a type IIR fluid-resistant surgical face mask throughout their shift; a type II surgical face mask may be worn by HCWs that are not involved in direct patient care/not at risk of splashing/spraying.
- HCWs should wear a type IIR fluid-resistant surgical face mask during any activities/procedures where there is a risk of blood, body fluids, secretions or excretions splashing or spraying onto their nose or mouth.
- Non-medical staff and HCWs off duty/out-with clinical areas should wear a face covering.
- All patients and visitors entering a healthcare setting should wear a face covering.
- Inpatients across all pathways should wear either a type II or IIR fluid-resistant surgical mask at all times if they can be tolerated and care is not compromised.

5.2 Face visors

The new Scottish COVID-19 addendum for acute settings (published 27th October 2020) recommends that eye/face protection should be worn at all times during direct contact in high-risk (red) pathways and this is always in combination with a face mask or respirator.[389] For low-risk (green) and medium-risk (amber) pathways, eye/face protection is only required if splashing or spraying with blood and/or body fluids is anticipated and again, this is always in combination with a face mask. Whilst the NIPCM Chapter 1 currently states that for SICPs a face visor can be used without a face covering to provide eye/face protection against splash and spray, at no point should a face visor be worn in place of a face mask when providing care on any of the three COVID-19 pathways. There is some evidence from experimental studies to

support that face visors alone are less effective than other forms of face protection at preventing influx of exhaled droplets/aerosols; these are covered in more detail in the **eye protection rapid review**. This is also the case for source control; an experimental study found that a face shield blocked only 2% of experimentally exhaled cough aerosols compared to 59% blocked by a fluid-resistant face mask and 51% blocked by a 3-ply cotton face covering.[534] The World Health Organization advises that face shields are considered to provide a level of eye protection only and should not be considered as an equivalent to masks with respect to respiratory droplet protection and/or source control.[20] The Health and Safety Executive (HSE) advises that in the event of severe shortages of medical masks, face shields may be considered as an alternative, but that they cannot be used as a substitute for respiratory protection.[535] Face visors may act as a barrier to face touching, however adherence to appropriate hand hygiene at all times as well as when donning and doffing PPE is essential to reduce the risk of indirect contact transmission.

Conclusion:

- Eye/face protection should be worn if splashing or spraying with blood and/or body fluids is anticipated.
- Eye/face protection should be worn when within 2 metres of patients in high-risk (red) pathways.
- A face visor should not be worn in place of a surgical face mask or respirator in the context of COVID-19.

5.3 Respiratory protective equipment (RPE)

The WHO defines an AGP as a medical or care procedure that creates the potential for airborne transmission of infections that may otherwise only be transmissible by the droplet route.[60] It should also be recognised that as well as producing aerosols, these procedures produce larger droplet particles.[61-63] During AGPs there is an increased risk of aerosol spread of infectious agents irrespective of the mode of transmission (contact, droplet, or airborne) and airborne precautions (FFP3 respirator and facial protection) must be implemented.[536] The evidence base underpinning AGP guidance is limited which has negatively impacted the ability to appraise novel procedures/procedures not currently on the AGP list for their applicability as AGPs. In recognition of this, Australian Government guidance has applied a risk-based approach for determining the use of RPE when caring for suspected/confirmed COVID-19

patients. Airborne precautions are advised for the clinical care of patients in inpatient hospital settings who have cognitive impairment, are unable to cooperate, or exhibit challenging behaviours (such as shouting). Airborne precautions are also advised where there are high numbers of COVID-19 patients AND a risk of challenging behaviours and/or unplanned AGPs, and; in settings where there is a high density of COVID-infected patients, particularly in wards or cohorted areas without optimal ventilation and where prolonged episodes of care are required.[537] In these scenarios, it is advised that respirators can be worn continuously for a single session of care but must be replaced if removed.[529] In reality, it may be difficult for HCWs to carry out a timely risk assessment based on the above, especially in triage areas, and subsequently there may be a tendency to opt for RPE as standard in specific care areas i.e. A&E, care of the elderly/mental health, older-style nightingale wards where options for patient placement are limited. This type of risk assessment may be of particular benefit when UK health and care settings move away from the use of green/amber/red ward allocations.

Further advocating the use of a risk assessment with regard to RPE and transmission risk, SAGE in April 2021 advised that if an unacceptable risk of transmission remains after rigorous application of the hierarchy of controls it may be necessary to consider the extended use of RPE for patient care in specific situations, taking into consideration the likelihood, duration and proximity of exposure to a COVID-19 case and what other measures have been applied in the setting.[24] This is in acknowledgement of the risk of aerosol transmission out with AGPs.

It is important to note that not all FFP3 respirators are fluid-resistant; valved respirators can be shrouded or unshrouded. Respirators with unshrouded valves are not considered to be fluid-resistant and therefore should be worn with a full face shield if blood or body fluid splashing is anticipated. This must be taken into consideration where FFP3 respirators are being used for protection against COVID-19 transmission.

Concern has also been raised regarding the suitability of respirators for providing source control, specifically where respirators are fitted with exhalation valves that offer no filtration of exhaled air. It is stated in the NIPCM that respirators must never be worn by an infectious patient due to the nature of the respirator filtration of incoming air rather than expelled air.[536] The ECDC, CDC, and WHO advise against the use of respirators with exhalation valves for source control of COVID-19.[538-540] A recent **ARHAI Scotland rapid review** that assessed respirators demonstrated consistency in the evidence that valved respirators should not be used for source control. It must therefore be acknowledged that there is a risk that staff later identified as infectious whilst wearing a valved respirator may have presented an exposure risk to patients and staff if within 2 metres. In Scottish healthcare settings, it is advised that

respirators are worn by HCWs when carrying out AGPs in medium and high risk pathways. At all other times, HCWs are expected to be wearing Type IIR fluid-resistant surgical face masks. However, in recognition of the anxiety felt by many HCWs with regards to PPE provision, Scottish guidance recommends that when prevalence is high, and where staff have concerns about potential exposure to themselves, they may choose to wear an FFP3 respirator rather than an FRSM when performing an AGP on a low-risk pathway patient; this is a personal PPE risk assessment.

Air sampling performed whilst carrying out tracheostomies on 8 COVID-19 patients that had subsequently tested PCR negative (2 negative tests) identified one positive air sample, collected in the vicinity of a patient that was 17 days post-symptom onset.[541] A patient of this type would have been placed on the high risk pathway in UK acute settings, meaning that RPE for AGPs would have been in place regardless and therefore the risk of AGP-mediated transmission to HCWs would have been mitigated. It is important that COVID status of a patient, even if recently tested negative, is reported to the receiving unit if discharged to a separate facility, and PPE risk assessment carried out.

Whilst an FFP3 respirator is the recommended RPE for use in the UK, it may not be reasonably practicable to use these if global supplies of FFP3 respirators are low during a pandemic. In this scenario, the WHO advise that an FFP2 could be used as an alternative. In March 2021, the UK Health and Safety Executive concluded in a rapid review that N95 respirators (used out with the UK) were comparable to FFP2 respirators and that both would provide comparable protection against coronavirus as long as the wearer was face-fit tested.[542]

Conclusion:

- Airborne precautions (FFP3 respirators) are required when performing AGPs on patients in the medium risk (amber) and high risk (red) pathways.
- HCWs may choose to wear an FFP3 respirator rather than an FRSM when performing an AGP on a low-risk pathway patient; this is a personal PPE risk assessment.
- The use of FFP2 respirators should be considered where there are shortages of FFP3 respirators.

5.4 UK PPE guidance

For general patient care (i.e. non-AGP situations), the first edition of the UK IPC pandemic COVID-19 guidance initially recommended type IIR FRSMs, disposable aprons and disposable gloves.[14] The decision to wear eye protection was based on risk assessment (but considered essential when carrying out AGPs). Fluid-resistant long sleeve gowns were recommended for management of confirmed cases and when carrying out AGPs.[14] FFP3 respirators were recommended when carrying out AGPs and when in high risk areas where AGPs are being conducted. The FFP3 recommendation was based on expert opinion from NERVTAG which recommended that airborne precautions should be implemented at all times in clinical areas considered AGP 'hot spots' e.g. Intensive Care Units (ICU), Intensive Therapy Units (ITU) or High Dependency Units (HDU) that are managing COVID-19 patients (unless patients are isolated in a negative pressure isolation room/or single room, where only staff entering the room need wear a FFP3 respirator).

The UK IPC pandemic COVID-19 guidance was updated on 2nd April 2020 with a move to PPE based on risk of exposure to possible (not suspected/confirmed) cases, with recommended ensembles for specific care areas/clinical situations.[543] The guidance stated that '*incidence of COVID-19 varies across the UK and risk is not uniform and so elements of the updated guidance are intended for interpretation and application dependent on local assessment of risk*'. While this was not in line with the evidence base to date for COVID-19 as presented in this rapid review, it was based on the potential challenges in establishing whether patients and individuals meet the case definition for COVID-19 prior to a face-to-face assessment or care episode. There was also a move towards sessional use of PPE considering the recognised global shortage of PPE stockpiles at the time and perhaps in recognition of the fact that the change in UK PPE recommendations were likely to result in greater use of PPE by a wider staff group which would deplete existing UK stocks.

UK PPE guidance published by PHE was updated on 20th August with the publication of IPC guidance for remobilisation of service in health and care settings.[544] A major change was the introduction of 3 patient pathways for COVID-19 which set out the PPE requirements for each area. The guidance was most recently updated on 21st January 2021, and the title renamed to '*Guidance for maintaining services within health and care settings*'.[545] Whilst sessional use of single use PPE/RPE items continued to be minimised in the recommendations, the guidance states that sessional or extended use of FFP3 respirators can be applied in the medium and high risk pathways where AGPs are undertaken for COVID-19 cohorted patients/individuals.

Scottish COVID-19 guidance (in the form of an addendum) was published in the NIPCM on 27th October 2020 and also includes the implementation of 3 patient pathways. There is a return to SICPs-based PPE, with PPE usage dictated by anticipated blood and/or body fluid exposure, and respirators only required for AGPs on patients in the amber and red pathways. As per the PHE UK guidance, there is no longer a requirement in Scottish settings for sessional PPE use, apart from FRSMs and face visors/eye protection which can be worn sessionally in a communal bay on the high risk pathway. In recognition of the anxiety felt by many HCWs with regards to PPE provision, Scottish guidance recommends that when prevalence is high, and where staff have concerns about potential exposure to themselves, they may choose to wear an FFP3 respirator rather than an FRSM when performing an AGP on a low-risk pathway patient; this is a personal PPE risk assessment.

Additionally, as per interim guidance published by the Scottish Government on June 23rd 2020, surgical face masks must be worn at all times by HCWs in clinical areas across all pathways within acute adult hospitals, community hospitals, and care homes for the elderly, to reduce the risk of source transmission.[533] This also applies to patients and visitors, who are required to wear a face covering at all times, and all staff out with clinical areas/not on duty who are also required to wear a face covering. Face mask/covering requirements were extended to include primary care (GP practices, dentists, opticians and pharmacies) and wider community care (including adult social or community care and adult residential settings, care home settings and domiciliary care) on 18th September.[533]

Reuse of PPE (FFP3/FF2/N95 respirators, fluid-resistant gowns or coveralls, goggles and face visors) as advised for periods of PPE shortages in a previous version of the IPC guidance in April 17th 2020, is no longer recommended in Scottish settings.

The Scottish and UK PPE guidelines remain in line with those issued by the World Health Organization.

The safety and efficacy of extended use or re-use of PPE has not been extensively studied. An evidence summary by ECRI (Emergency Care Research Institute), a US company that evaluates medical devices, evaluated 21 laboratory studies and concluded that extended use (i.e. sessional use) of N95 respirators was preferable to reuse.[546] Mechanical failure (e.g. broken straps and poor sealing between the mask and the user's face) following only a few reuses was common across a number of FDA-cleared N95 respirators. The reported pathogen transfer risk from contact during donning and doffing during reuse was considered to be higher than the risk from sessional wear. Use of surgical masks or similar disposable covers over N95s during sessional wear were unlikely to result in significant adverse effects. Reuse would

require disinfection however loss of filter performance was reported with some common disinfection methods. The methods for disinfection included humid heat, chemical disinfection, and ultraviolet germicidal irradiation (UVGI). The ECRI report summarises the findings from a number of decontamination studies conducted; steam sterilisation required 10 minutes at a minimum of 121°C to be effective however it may damage polymer fibres in the filter and compromise performance; chemical disinfection was limited by the risk of toxicity and chemical incompatibility with filter materials; UVGI penetration may be incomplete in multi-layered N95 filters, which has been evidenced experimentally.[547] UVGI is capable of inactivating coronaviruses including MERS-CoV and SARS-CoV however these tests were not conducted on any type of PPE.[548] UV radiation degrades polymers which presents the possibility that UVGI exposure may reduce the efficacy of respirators.[549] A previous study demonstrated degradation of 4 different types of N95 respirators at doses of 120-950 J/cm^2.[550] Attempts at using steam sterilisation of FFP respirators has shown promise however rigorous testing in line with EN standards for respirator efficacy is required.[551] In a separate study, heat treatment at 70°C at either 0% or 50% humidity did not appear to damage N95 masks nor compromise fit performance, however this study only measured the efficacy of this method at removing SARS-CoV-2 from respirators by using respirator material that had been cut into 1cm^2 pieces.[552] None of the eight different decontamination methods that were tested on different N95 respirator models were suitable, failing in terms of ability to penetrate the filters and/or as a result of damage to the respirators.[553] The methods included UVGI, ethylene oxide, hydrogen peroxide gas plasma, hydrogen peroxide vapour, microwave-oven-generated steam, bleach, liquid hydrogen peroxide, and moist heat incubation (pasteurization). Disinfection using aerosolised peracetic acid and hydrogen peroxide vapour was found to be effective at reducing contamination of a surrogate coronavirus bacteriophage on N95 respirators.[554] Use of vaporised hydrogen peroxide was also found to be suitable for N95 respirator decontamination using an experimental inoculum of SARS-CoV-2 with a cycle threshold value of 20–22.[555] Notably, the safety of these chemicals for this purpose has not been tested and decontamination should be tested on naturally contaminated PPE, as experimental contamination may not be representative of the levels of contamination experienced in real-life clinical scenarios.

UK IPC pandemic COVID-19 guidance has never recommended decontamination of respirators.[543] Respirators should be discarded if they become moist, visibly soiled, damaged, or become hard to breathe through. The ECDC recommends that, where reuse of respirators is considered as a last resort option to economise on use of PPE, the risk of the surface of the

respirator becoming contaminated by respiratory droplets is considered to be lower when it is covered with a visor.[556] However this ensemble is dependent on a plentiful supply of visors.

As highlighted in the ECRI report, the reported pathogen transfer risk from contact during donning and doffing during reuse was considered to be higher than the risk from sessional wear.[546] Unfortunately there is no evidence available to assess the impact on filtration efficacy or the risk of transmission associated with reuse of RPE in clinical settings. A study that assessed efficacy of type IIR FRSMs and N95 respirators that were worn sessionally and reused did not include a reliable control group for comparison which prevented assessment of the efficacy of continuous wear/reuse.[557] RPE was reported to be stored between shifts in a paper bag in lockers; the extent of reuse was not reported. Compared with continuous use of FRSMs, respirators were associated with more problems for the wearer including significantly greater discomfort, trouble communicating with the patient, headaches, difficulty breathing, and pressure on the nose.[557] The WHO '*Rational use of PPE for COVID-19*' mentions that respirators can and have previously been used for extended periods of time to treat multiple patients with the same diagnosis.[558] Whilst WHO state that there is evidence to support respirators maintaining their protection over longer periods of time, it may not be comfortable to use one respirator for longer than 4 hours and this should be avoided[558] as reuse may increase the potential for contamination and contact transmission of infectious agents (not just SARS-CoV-2). This risk must be balanced against the need to provide respiratory protection for HCWs providing care and to those performing AGPs. To reduce the risk of transmission associated with PPE reuse it is essential that HCWs demonstrate stringent compliance with all other infection control precautions, hand hygiene, and environmental decontamination. Irrespective of the measure implemented, HCWs must have IPC education and training on the correct use of PPE and other IPC precautions, including demonstration of competency in appropriate procedures for donning and doffing PPE and hand hygiene. These issues are for consideration by the Health and Safety Executive (HSE). The HSE approved the sessional use and reuse of PPE in the UK for COVID-19 and expects NHS Boards to have an agreed action plan that includes consideration of all measures to manage usage effectively.

Conclusion:

- PPE should be single-use unless otherwise stated by the manufacturer.
- Continuous use of surgical face masks in clinical areas (or face coverings in non-clinical areas) is required in line with physical distancing measures to reduce the risk of source transmission.

- Consideration should be given to the unit wide application of airborne precautions where the number of cases of COVID-19 in amber and red pathways requiring AGPs increases and patients/individuals cannot be managed in single or isolation rooms.
- In periods of PPE shortages, sessional use of respirators is preferred over reuse.
- In periods of PPE shortages, the decision to reuse PPE (respirators, fluid-resistant gowns or coveralls, goggles and face visors) should be based on a risk assessment considering the care activities, patient population, and the state of the PPE in question.

6. Hand hygiene

Most articles identified recommend that hand hygiene should be performed, however many do not specify the product(s) to be used in preventing the transmission of SARS-CoV-2. A number of guidance documents provide specific recommendations which differ only slightly.[8, 12, 16] WHO and Public Health England support the use of soap and water, and alcohol-based hand rub (ABHR) when soap and water is not available and when hands are not visibly soiled.[12, 16] Experimental evidence has shown that commercially-available ABHRS and WHO ABHR formulations are effective at inactivating SARS-CoV-2 within a contact time of 30 seconds.[559, 560] Commercially-available ABHRs have also shown efficacy against other coronaviruses included SARS-CoV and MERS-CoV.[559, 561]

Conclusion:

- Hand hygiene should be performed with soap and water or, when hands are not visibly soiled, with ABHR.

7. Survival in the environment

A number of environmental sampling studies of rooms/areas occupied by COVID-19 patients and surrounding areas sampled various locations prior to environmental cleaning; viral RNA was found on multiple surfaces including the bed, bed sheets, bed rail, locker, chair, computer table, keyboard, light switches, sink, taps, floor and staff shoes, window ledge, PPE storage area, hand sanitiser dispensers, air outlet fans, elevator buttons, as well as the toilet bowl surface and handle, door handle, and medical equipment (ventilators, monitors, blood pressure cuffs, thermometers, drainage bags, high flow oxygen generator, endotracheal tube, infusion pumps).[26-29, 31, 35-38, 43, 45-47, 49, 56, 57, 475, 562-572] Personal items such as mobile phones, TV remotes, towels and toothbrushes were also contaminated.[27, 45, 56, 57, 563] Overall, positive rates were significantly higher in medical areas compared to office areas and buffer rooms for donning PPE; contamination in these areas was found on telephones, desktops, keyboards, computer mice and water machine buttons.[35, 568] Sampling carried out prior to environmental cleaning across patient care areas and non-patient care areas of an emergency department revealed positive samples in patient care areas only (from stretchers, pulse oximeters, blood pressure cuffs, plastic screens between patients, and the floor).[573] A study that sampled multiple surfaces within an emergency triage unit and a sub-intensive care ward identified positive samples on 2 CPAP helmets only.[574] It is possible that environmental cleaning, carried out 4 hours prior, may have impacted results. Environmental sampling studies are often limited as they omit information regarding frequency of environmental cleaning, or conduct sampling immediately following cleaning.[575, 576] Viable virus has been detected in one study from samples collected from the surfaces of fixtures, fittings and medical equipment in COVID-19 patient rooms[27] but most studies have failed to demonstrate viability.[47, 56, 568, 574] The potential effect of disease progression and viral shedding on environmental contamination has not been investigated extensively, however one study has demonstrated a significant correlation between viral load ranges in clinical samples and positivity rate of environmental samples ($p < 0.001$).[577] When the viral load of clinical samples was higher than or equal to 3 log copies/ml, environmental contamination with SARS-CoV-2 could be detected. However, the sample size in this study was small and further research is required to confirm these findings. Environmental contamination was detected in two hotel rooms occupied by quarantined cases that were pre-symptomatic during their stay, which highlights the risk of environmental contamination from shedding in the pre-symptomatic phase.[578] Viral RNA contamination of high touch surfaces in public places (shops, banks, fuel station) has also been demonstrated but viability was not tested.[579] In general, sampling studies highlight the potential for environmental

contamination, particularly of frequently-touched areas, but the risk of acquiring infection from contaminated environmental sites remains unknown. Very few studies have tested viability of PCR-positive samples obtained from environmental swabbing. Sampling of surfaces considered to be low touch (tops of door frames, tops of shelving units) in a number of long term care facilities in Canada generated positive PCR samples but viability could not be demonstrated in culture; care activities in these settings were not provided in detail.[34] An in-vivo study tested the viability of SARS-CoV-2 under a number of experimental conditions and found that cells remained viable for 3-5 days at room temperature.[580] In light of limited data for SARS-CoV-2 regarding survival time in the environment, evidence was assessed from studies conducted with human coronaviruses including MERS-CoV and SARS-CoV, and human coronavirus 229E. From largely experimental studies, human coronaviruses are capable of surviving on inanimate objects and can remain viable for up to 5 days at temperatures of 22-25°C and relative humidity of 40-50% (which is typical of air conditioned indoor environments).[11, 129, 581-584] Experimental evidence indicates that SARS-CoV-2 survival in the environment is negatively impacted by increasing temperature.[585-587] Survival is also dependent on the surface type.[581, 587-589] Experimental studies using SARS-CoV-2 strains have reported viability on plastics for up to 120 hours, for 72 hours on stainless steel, 120 hours on glass,[590] 24 hours on acrylic,[588] and up to 8 hours on carpet, copper and upholstery.[588, 591, 592] Viability was quantified by end-point titration on Vero E6 cells. An experimental study conducted with human coronavirus 229E found that the virus persisted on Teflon, PVC, ceramic tiles, glass, and stainless steel for at least 5 days (and 3 days for silicon rubber) at 21°C and a relative humidity of 30-40%.[593] Another experimental study performed using 3 variants of SARS-CoV-2 (B.1.1.7, B.1.351 and their common predecessor, EPI_ISL_407073) demonstrated that the virus remained viable for up to 7 days at 19°C and 57% relative humidity following inoculation on stainless steel coupons, with no significant difference in viability once the inoculums had dried ($p = 0.12$). Significantly higher units of the B.1.1.7 and B.1.351 variants were recovered compared to their common predecessor during the drying process ($p = 0.01$), however, further research in this area is necessary to determine the implications of these findings.[594] Infectivity of the persistent viral cells was demonstrated experimentally using a plaque assay in both of these experimental studies, however the infectivity of surface-contaminating SARS-CoV-2 in real-life conditions remains unknown. Experimental testing in the dark (zero UV) found that SARS-CoV-2 could survive for prolonged periods on multiple surface types however the negation of UV is not representative of real-life scenarios and the results of such experiments must be interpreted with caution.[595] Another experimental study detected viable SARS-CoV-2 virus for up to 7 days on hydrophobic surfaces (i.e. stainless steel, Tyvek, disposable gowns, bank notes and surgical masks) and 3 days on hydrophilic surfaces (i.e. cotton and polyester

shirts) at 21°C and average relative humidity of 45%.[589] Survival of human coronaviruses and surrogates in water is influenced by temperature (viral inactivation increases with increasing temperatures) and organic or microbial pollution.[596] A 99.9% viral titre reduction was observed after 2-3 days in waste water in an experimental study using human coronavirus 229E, suggesting low survivability in waste water.[597] Samples taken from the treated sewage outlets of a number of COVID-19 Chinese hospitals were negative.[598, 599] Samples taken (with varying methodology) from external water treatment plants in the UK, Netherlands, France, Spain, the US, and Canada) tested positive in line with the detection of cases in the population which suggests that RT-PCR analysis of sewage could be a potential surveillance tool.[600-608] Testing of sewage treatment works is now being carried out by the Scottish Environment Protection Agency (SEPA) to determine if such data exists to generate a surveillance system. A report prepared for SAGE in November 2020 and April 2021, advised that UK wastewater surveillance programs for COVID-19 have been in place across England, Scotland and Wales since early summer 2020 and is a reliable, timely and cost-effective surveillance method, particularly during low prevalence, and to identify local variants.[609, 610] In Orkney (population equivalent 7750 in the catchment area), virus was detected in the wastewater where less than 10 positive cases had been recorded.[609] Wastewater sampling in Switzerland identified the presence of mutations indicative of the new UK variant B.1.1.7 in early December 2020 prior to detection of the first clinical sample in Switzerland.[611] In Canada, it was found retrospectively that wastewater sampling accurately predicted a surge in community cases 48 hrs prior to their detection.[608] There is currently no evidence that COVID-19 is transmitted from sewage/grey water or contaminated drinking water.[609, 612]

Conclusion:

- Due to the uncertainty regarding the environmental survivability of SARS-CoV-2 in real-life conditions, it is essential that the environment is clutter free and frequency of routine cleaning is increased, particularly frequently-touched surfaces.

8. Environmental decontamination

Evidence for cleaning of the care environment for COVID-19 is limited; studies that evaluate the susceptibility of coronaviruses to cleaning/disinfectant products differ by their methodology and often use animal coronaviruses in experimental conditions.[129, 561, 581] An experimental study using a SARS-CoV isolate, tested three different surface disinfectants but all required over 30 minutes exposure time to inactivate the virus to levels below detection.[561] Limited evidence

suggests that coronaviruses are susceptible to chlorine-based disinfectants and ethanol-based antiseptics.[581, 613, 614] Kampf et al summarised the efficacy of various disinfectants against both human and animal coronaviruses and found that a concentration of 0.1% sodium hypochlorite was effective in 1 minute and, for the disinfection of small surfaces, 62-71% ethanol revealed a similar efficacy.[581] Laboratory analysis has shown that SARS-CoV-2 can be inactivated in vitro in under 1 minute using 1000mg/L available chlorine.[615] Experimental testing has shown SARS-CoV-2 on inanimate surfaces (stainless steel, plastic, glass, PVC, cardboard) can be inactivated by 70% ethanol, 70% isopropanol, and 0.1% hydrogen peroxide.[614] Specifically, complete inactivation was observed in 30 seconds with ethanol and isopropanol, and in 60 seconds with 0.1% hydrogen peroxide; complete viral inactivation on cotton fabric was observed after 30 seconds with 0.1% sodium laureth sulphate, which is a surfactant present in almost all household cleaning/ personal hygiene agents (e.g. dishwashing liquid, hand soaps and shampoos).[614] Unfortunately there is a paucity of evidence regarding the efficacy of detergents at deactivating SARS-CoV-2, and due to the novel nature of this infectious agent there is an assumption that only disinfectants will be effective. In vitro analysis of a number of laboratory detergents used for biochemical analysis demonstrated some efficacy against SARS-CoV-2 however the detergents were not designed for environmental cleaning.[616] The CDC states that, in addition to physical removal of SARS-CoV-2, surface cleaning is likely to degrade the virus, while surfactants in cleaners/detergents can disrupt and damage the membrane of an enveloped virus like SARS-CoV-2.[617]

The WHO recommends that, for coronaviruses, commonly used hospital-level disinfectants such as sodium hypochlorite (at a concentration of 0.5%) are effective for cleaning environmental surfaces, and 70% ethanol is suitable for disinfecting small surfaces.[16] A sampling study found that twice daily cleaning of frequently-touched areas using 5000 ppm of sodium dichloroisocyanurate (a source of free chlorine) resulted in negative swab results for COVID-19 in isolation rooms that had just been cleaned; samples taken from rooms prior to cleaning had multiple positive samples from frequently-touched areas.[562] Similar results were reported from a Chinese hospital in which surfaces were routinely wiped with 1000 mg/L chlorine-containing disinfectant every 4 hours in isolation ICUs and every 8 hours in general isolation wards; none of the environmental samples in these areas tested positive for SARS-CoV-2 contamination.[598] Negative results were also found from sampling of 90 surfaces following disinfection in a Wuhan hospital dedicated to treating COVID-19 patients, in which a comprehensive environmental decontamination protocol was implemented.[357] It consisted of chlorine dioxide air disinfection 4 times a day for 2 hours at a time in COVID-19 wards, irradiation of empty wards with UV light once per day for 1 hour, ultra-low volume spraying of

chlorine dioxide (500mg/L) for air disinfection in public areas, and surfaces/objects were 'wrapped' with chlorine-containing disinfection solution (1000mg/L) twice a day.

For situations where health and care settings are at capacity and/or have no breaks in admissions or bed occupancy, the opportunity to conduct a terminal clean or a deep clean may be limited. Solutions to this may include modification to the deep clean regime to allow as high a level of decontamination to be carried out during constant occupancy as possible.

In light of the concern raised regarding aerosol transmission following the identification of positive air samples from hospital rooms,[38, 40, 56, 562] alternative decontamination techniques that offer air decontamination should be explored. Air disinfection using ultraviolet-C light, termed ultraviolet germicidal irradiation (UVGI) is accomplished via several methods: irradiating the upper-room air only, irradiating the full room (when the room is not occupied or protective clothing is worn), and irradiating air as it passes through enclosed air-circulation and heating, ventilation, and air-conditioning (HVAC) systems.[618] UVGI is also used in self-contained room air disinfection units. The overarching limitation of most UVGI systems is that the room must be vacated whilst disinfection is taking place; any reductions in aerosol/surface contamination will be short-lived as once the room is re-occupied, potentially infectious viral particles may again be circulating. UVGI air decontamination should therefore not be used as a replacement for optimum ventilation provision, however it may have a future use for terminal decontamination and/or in rooms in which AGPs are carried out where improvements to the existing ventilation provision are not possible. One before/after observational study that tested a UVC robot within an American long term care facility had respiratory system infection rates as an outcome measure however the methodological limitations meant that causation could not be proven; there was no certainty that the observed respiratory system infection rate decreases were due to the UVC treatment alone (and not in part due to the manual cleaning that preceded the UCGI treatment).[619] A number of experimental studies have tested the efficacy of UVGI (specifically UVC) at inactivating SARS-CoV-2;[590, 620-626] all of the experimental studies reported on surface decontamination, none of the studies assessed air decontamination. It was not possible to summarise the collective findings of these studies due to the heterogeneity in methodology; the dose of UV, duration of exposure, and distance between the lamp and test isolate varied. Individually, these studies demonstrated efficacy under their varying experimental conditions. In one study, a dose of 1.8mW/cm2 UVC was effective at inactivating experimentally contaminated glass, plastic and gauze.[626] Another *in vitro* study reported a 10-minute exposure (34.9 mJ/cm2) on glass and plastic, and 15 minutes (52.5 mJ/cm2) on stainless steel was required to lower viral titre to below the level of detection [620] Further research into UVC decontamination of SARS-CoV-2 is warranted in real-life trials. A review of UV decontamination technology by HPS

recommended that UV light systems can be used as an additional measure when performing terminal room decontamination.[627] However, as surface cleaning is required prior to UVC disinfection, UVC technology will not offer any time-saving benefits and can only be seen as an adjunct to standard environmental decontamination.

The latest version of the PHE IPC guidance advises that low risk (green) COVID-19 pathways can revert to general purpose detergents for routine cleaning, as opposed to widespread use of disinfectants.[545] The Scottish COVID-19 addendum further advises that the use of general purpose detergent for cleaning in the low risk pathway is sufficient with the exception of isolation/cohort areas where patients with a known or suspected infectious agent are being nursed.[389]

Conclusion:

- Frequency of environmental cleaning/decontamination in all health and care settings should be increased to at least twice daily, focusing on frequently-touched areas.
- A general purpose detergent should be used for routine cleaning in low risk (green) pathways and in health and care settings that are COVID-19-free.
- A combined detergent/disinfectant solution at a dilution of 1,000 parts per million available chlorine (ppm available chlorine (av.cl.)) should be used for transmission-based environmental decontamination as per the NIPCM, in medium- and high-risk COVID-19 pathways and any settings experiencing cases/outbreaks. Small surfaces, and those which cannot be cleaned by chlorine-based agents, can be disinfected with 70% ethanol.
- Where terminal cleaning cannot be carried out due to constant occupancy, a modified enhanced clean should be carried out where possible.
- Further research is required to determine the effectiveness of UVC technology for decontamination of SARS-CoV-2.

9. Areas for further research

An overarching limitation of all identified evidence is the novel nature of SARS-CoV-2 and the limited ability for robust research at the early stages of an outbreak.

More work is needed to improve and develop culture techniques to allow determination of the viability of viral particles detected in clinical and environmental samples. This will assist with

determination of the infectious dose and will provide insight into the duration of infectivity, particularly in relation to the prolonged viral shedding that is observed in respiratory and faecal samples.

Of particular importance is the need to undertake further research to determine the potential contribution of aerosol transmission of respiratory viruses (not limited to SARS-CoV-2), acknowledging a spectrum of particle sizes, which is understandably beyond the scope of a rapid review.

Further research is required to determine the extent of atypical presentations, pre-symptomatic, and asymptomatic transmission and the overall impact of these on transmission. A robust epidemiological evidence base will assist with the development of infection control measures that are targeted and evidence-based.

Assessment of the efficacy of UVGI and other novel decontamination technologies for environmental decontamination and for the decontamination of PPE would inform COVID-19 IPC guidance and provide reassurance for health and care workers. Studies investigating the efficacy of detergents for environmental cleaning would provide a clear evidence base to support a move away from chlorine-based disinfection in the medium risk pathway.

10. Limitations

An overarching limitation of all identified evidence is the novel nature of SARS-CoV-2 and the limited ability for robust research during a pandemic. Most papers highlight the need for further research.

There are a number of inherent limitations related to rapid reviews, including risk of publication bias, potential omission of key evidence, and the provision of a descriptive analysis of evidence rather than a qualitative analysis. There is a risk of duplication of reported cases as case reports become part of a larger body of evidence.

Consequently, conclusions from this rapid review should be interpreted with caution and considered alongside additional streams of evidence (for example local epidemiological data.

Appendix 1

Search Strategies used for academic databases.

The search terms for searches conducted from 5th March 2020 until 14th September 2020 were as follows:

1. COVID-19.mp.
2. SARS-CoV-2.mp.
3. 2019-nCoV.mp.
4. novel coronavirus.mp.
5. exp coronavirus/
6. 1 or 2 or 3 or 4 or 5
7. exp infection control/
8. exp disinfection/
9. exp decontamination/
10. exp personal protective equipment/
11. surgical mask?.mp.
12. hand hygiene.mp.
13. clean*.mp.
14. transmission.mp.
15. 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15
16. 6 and 16
17. limit 17 to English language
18. limit 18 to yr="2020 -Current"

Search terms for 21st September 2020 until 22nd February 2021 were as follows:

1. (coronavirus or corona virus or ncov* or covid* or 2019-ncov or ncov19 or ncov-19 or 2019-novel CoV or sars-cov2 or sars-cov-2 or sarscov2 or sarscov-2 or Sars-coronavirus2 or Sars-coronavirus-2 or SARS-like coronavirus* or coronavirus-19 or covid19 or covid-19).mp.
2. infection control.ti,kw,ab.
3. disinfection.ti,kw,ab.
4. decontamination.ti,kw,ab.
5. personal protective equipment.ti,kw,ab.
6. ppe.ti,kw,ab.
7. surgical mask*.ti,kw,ab.

8. respiratory protective device*.ti,kw,ab.
9. respirator.ti,kw,ab.
10. FFP3.ti,kw,ab.
11. eye protective device*.ti,kw,ab.
12. goggles.ti,kw,ab.
13. face shield*.ti,kw,ab.
14. visor*.ti,kw,ab.
15. safety glasses.ti,kw,ab.
16. hand hygiene.ti,kw,ab.
17. clean*.ti,kw,ab.
18. transmission.ti,kw,ab.
19. 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18
20. 1 and 19
21. limit 20 to english language
22. limit to human
23. limit 22 to dd=_____-_____

Search terms for 1st March 2021 onwards were as follows:

1. (coronavirus or corona virus or ncov* or covid* or 2019-ncov or ncov19 or ncov-19 or 2019-novel CoV or sars-cov2 or sars-cov-2 or sarscov2 or sarscov-2 or Sars-coronavirus2 or Sars-coronavirus-2 or SARS-like coronavirus* or coronavirus-19 or covid19 or covid-19).mp.
2. infection control.ti,kw,ab.
3. disinfection.ti,kw,ab.
4. decontamination.ti,kw,ab.
5. personal protective equipment.ti,kw,ab.
6. ppe.ti,kw,ab.
7. surgical mask*.ti,kw,ab.
8. respiratory protective device*.ti,kw,ab.
9. respirator.ti,kw,ab.
10. respirators.ti,kw,ab.
11. FFP3*.ti,kw,ab.
12. eye protective device*.ti,kw,ab.
13. goggles.ti,kw,ab.

14. face shield*.ti,kw,ab.
15. visor*.ti,kw,ab.
16. safety glasses.ti,kw,ab.
17. hand hygiene.ti,kw,ab.
18. clean*.ti,kw,ab.
19. transmission.ti,kw,ab.
20. airborn*.ti,kw,ab.
21. aerosol*.ti,kw,ab.[1]
22. 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21
23. 1 and 20
24. limit 21 to english language
25. limit 22 to dd= _____ - _____[2]

Search strategy used for pre-print database.

"infection control" OR disinfection OR decontamination OR "personal protective equipment" OR ppe OR "surgical mask" OR "respiratory protective device" OR respirator OR respirators OR FFP3 OR "eye protective device" OR goggles OR "face shield" OR visor OR "safety glasses" OR "hand hygiene" OR clean* OR "transmission" OR airborn* OR aerosol*

Date limited to previous week.

[1] Search areas adjusted to ".ti,kf,ab." for search on Medline

[2] Date limit term changed to "dt=" for search on Medline

References

1. To KKW, Tsang OTY, Chik-Yan Yip C, et al. Consistent detection of 2019 novel coronavirus in saliva. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America 2020; 12.
2. Wang FS and Zhang C. What to do next to control the 2019-nCoV epidemic? *The Lancet* 2020; 395: 391-393. Note.
3. Rothan HA and Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. *Journal of Autoimmunity* 2020: 102433. Review.
4. Xia J, Tong J, Liu M, et al. Evaluation of coronavirus in tears and conjunctival secretions of patients with SARS-CoV-2 infection. *Journal of Medical Virology* 2020; 26: 26.
5. Peeri NC, Shrestha N, Rahman MS, et al. The SARS, MERS and novel coronavirus (COVID-19) epidemics, the newest and biggest global health threats: what lessons have we learned? *International journal of epidemiology* 2020; 22.
6. Yang Y, Shang W and Rao X. Facing the COVID-19 outbreak: What should we know and what could we do? *Journal of medical virology* 2020; 24.
7. Lai CC, Shih TP, Ko WC, et al. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. *International Journal of Antimicrobial Agents* 2020; (no pagination). Review.
8. Jin YH, Cai L, Cheng ZS, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). *Military Medical Research* 2020; 7 (1) (no pagination). Review.
9. Wax RS and Christian MD. Practical recommendations for critical care and anesthesiology teams caring for novel coronavirus (2019-nCoV) patients. *Canadian Journal of Anesthesia* 2020. Review.
10. Wu YC, Chen CS and Chan YJ. Overview of The 2019 Novel Coronavirus (2019-nCoV): The Pathogen of Severe Specific Contagious Pneumonia (SSCP). *Journal of the Chinese Medical Association : JCMA* 2020; 11.
11. Li JY, You Z, Wang Q, et al. The epidemic of 2019-novel-coronavirus (2019-nCoV) pneumonia and insights for emerging infectious diseases in the future. *Microbes and infection* 2020; 19.

12. Public Health England. COVID-19: infection prevention and control guidance. 6 March 2020 2020.

13. Department of Health Ireland. COVID-19 (Coronavirus): Advice. How COVID-19 (Coronavirus) spreads. 10 March 2020 2020.

14. Department of Health and Social Care (DHSC) PHWP, Public Health Agency (PHA) Northern Ireland, Health Protection Scotland (HPS), Public Health England,. *COVID-19; Guidance for infection prevention and control in healthcare settings*. 2020.

15. Centres for Disease Control and Prevention. Coronavirus Disease 2019 (COVID-19) – How COVID-19 Spreads. , **https://www.cdc.gov/coronavirus/2019-ncov/about/transmission.html** (2020).

16. World Health Organization. Infection prevention and control during health care when coronavirus (nCoV) infection is suspected. Interim guidance. 25 January 2020 2020.

17. World Health Organization. Transmission of SARS-CoV-2: implications for infection prevention precautions - Scientific Brief. . 9 July 2020 2020.

18. European Centre for Disease Prevention and Control. Infection prevention and control and preparedness for COVID-19 in healthcare settings. Sixth update – 9 February 2021. . 9 February 2021 2021.

19. Centers for Disease Control and Prevention. *Scientific brief: SARS-CoV-2 and potential airborne transmission*. 5 October 2020 2020.

20. World Health Organization. *Mask use in the context of COVID-19. Interim guidance, 1 December 2020.* . 1 December 2020 2020.

21. Miller SL, Nazaroff WW, Jimenez JL, et al. Transmission of SARS-CoV-2 by inhalation of respiratory aerosol in the Skagit Valley Chorale superspreading event. *Indoor Air* 2020 2020/09/27. DOI: 10.1111/ina.12751.

22. Kwon KS, Park JI, Park YJ, et al. Evidence of Long-Distance Droplet Transmission of SARS-CoV-2 by Direct Air Flow in a Restaurant in Korea. *J Korean Med Sci* 2020; 35: e415. 2020/12/02. DOI: 10.3346/jkms.2020.35.e415.

23. Li Y, Qian H, Hang J, et al. Evidence for probable aerosol transmission of SARS-CoV-2 in a poorly ventilated restaurant. . *medRxiv* 2020; PRE-PRINT.

24. Scientific Advisory Group for Emergencies. *HOCI and EMG: Masks for healthcare workers to mitigate airborne transmission of SARS-CoV-2, 25 March*. 23 April 2021 2021.

25. Faridi S, Niazi S, Sadeghi K, et al. A field indoor air measurement of SARS-CoV-2 in the patient rooms of the largest hospital in Iran. *Sci Total Environ* 2020; 725: 138401. 2020/04/14. DOI: 10.1016/j.scitotenv.2020.138401.

26. Jerry J, O'Regan E, O'Sullivan L, et al. Do established infection prevention and control measures prevent spread of SARS-CoV-2 to the hospital environment beyond the patient room? *J Hosp Infect* 2020 2020/06/27. DOI: 10.1016/j.jhin.2020.06.026.

27. Ahn JY, An S, Sohn Y, et al. Environmental contamination in the isolation rooms of COVID-19 patients with severe pneumonia requiring mechanical ventilation or high-flow oxygen therapy. *J Hosp Infect* 2020 2020/08/24. DOI: 10.1016/j.jhin.2020.08.014.

28. Wei L, Lin J, Duan X, et al. Asymptomatic COVID-19 Patients Can Contaminate Their Surroundings: an Environment Sampling Study. *mSphere* 2020; 5 2020/06/26. DOI: 10.1128/mSphere.00442-20.

29. Kim UJ, Lee SY, Lee JY, et al. Air and Environmental Contamination Caused by COVID-19 Patients: a Multi-Center Study. *J Korean Med Sci* 2020; 35: e332. 2020/09/23. DOI: 10.3346/jkms.2020.35.e332.

30. Declementi M, Godono A, Mansour I, et al. Assessment of air and surfaces contamination in a COVID-19 non-Intensive Care Unit. *Med Lav* 2020; 111: 372-378. 2020/10/31. DOI: 10.23749/mdl.v111i5.9991.

31. Wei L, Huang W, Lu X, et al. Contamination of SARS-CoV-2 in patient surroundings and on personal protective equipment in a non-ICU isolation ward for COVID-19 patients with prolonged PCR positive status. *Antimicrob Resist Infect Control* 2020; 9: 167. 2020/10/31. DOI: 10.1186/s13756-020-00839-x.

32. Dumont-Leblond N, Veillette M, Mubareka S, et al. Low incidence of airborne SARS-CoV-2 in acute care hospital rooms with optimized ventilation. *Emerg Microbes Infect* 2020: 1-36. 2020/11/19. DOI: 10.1080/22221751.2020.1850184.

33. Lane MA, Brownsword EA, Babiker A, et al. Bioaerosol sampling for SARS-CoV-2 in a referral center with critically ill COVID-19 patients March-May 2020. *Clin Infect Dis* 2021 2021/01/29. DOI: 10.1093/cid/ciaa1880.

34. Dumont-Leblond N, Veillette M, Bherer L, et al. Positive no-touch surfaces and undetectable SARS-CoV-2 aerosols in long-term care facilities: An attempt to understand the contributing factors and the importance of timing in air sampling campaigns. *Am J Infect Control* 2021 2021/02/16. DOI: 10.1016/j.ajic.2021.02.004.

35. Wu S, Wang Y, Jin X, et al. Environmental contamination by SARS-CoV-2 in a designated hospital for coronavirus disease 2019. *Am J Infect Control* 2020 2020/05/15. DOI: 10.1016/j.ajic.2020.05.003.

36. Razzini K, Castrica M, Menchetti L, et al. SARS-CoV-2 RNA detection in the air and on surfaces in the COVID-19 ward of a hospital in Milan, Italy. *Sci Total Environ* 2020; 742: 140540. 2020/07/04. DOI: 10.1016/j.scitotenv.2020.140540.

37. Ding Z, Qian H, Xu B, et al. Toilets dominate environmental detection of severe acute respiratory syndrome coronavirus 2 in a hospital. *Sci Total Environ* 2020; 753: 141710. 2020/09/07. DOI: 10.1016/j.scitotenv.2020.141710.

38. Chia PY, Coleman K, Tan YK, et al. Detection of air and surface contamination by severe acute respratory syndrome coronavirus 2 (SARS-CoV-2) in hospital rooms of infected patients. *medRxiv* 2020; NOT PEER REVIEWED.

39. Ong SWX, Tan YK, Coleman KK, et al. Lack of viable SARS-CoV-2 among PCR-positive air samples from hospital rooms and community isolation facilities. *Infect Control Hosp Epidemiol* 2021: 1-17. 2021/01/26. DOI: 10.1017/ice.2021.8.

40. Liu Y, Ning Z, Chen Y, et al. Aerodynamic analysis of SARS-CoV-2 in two Wuhan hospitals. *Nature* 2020 2020/04/28. DOI: 10.1038/s41586-020-2271-3.

41. Passos RG, Silveira MB and Abrahao JS. Exploratory assessment of the occurrence of SARS-CoV-2 in aerosols in hospital facilities and public spaces of a metropolitan center in Brazil. *Environ Res* 2021; 195: 110808. 2021/01/30. DOI: 10.1016/j.envres.2021.110808.

42. Stern RA, Koutrakis P, Martins MAG, et al. Characterization of hospital airborne SARS-CoV-2. *Respir Res* 2021; 22: 73. 2021/02/28. DOI: 10.1186/s12931-021-01637-8.

43. Guo ZD, Wang ZY, Zhang SF, et al. Aerosol and Surface Distribution of Severe Acute Respiratory Syndrome Coronavirus 2 in Hospital Wards, Wuhan, China, 2020. *Emerg Infect Dis* 2020; 26: 1583-1591. 2020/04/11. DOI: 10.3201/eid2607.200885.

44. Kenarkoohi A, Noorimotlagh Z, Falahi S, et al. Hospital indoor air quality monitoring for the detection of SARS-CoV-2 (COVID-19) virus. *Sci Total Environ* 2020; 748: 141324. 2020/08/18. DOI: 10.1016/j.scitotenv.2020.141324.

45. Moore G, Rickard H, Stevenson D, et al. Detection of SARS-CoV-2 within the healthcare environment: a multicentre study conducted during the first wave of the COVID-19 outbreak in England. *MedRxiv* 2020; PREPRINT.

46. Tan L, Ma B, Lai X, et al. Air and surface contamination by SARS-CoV-2 virus in a tertiary hospital in Wuhan, China. *Int J Infect Dis* 2020 2020/07/31. DOI: 10.1016/j.ijid.2020.07.027.

47. Ben-Schmuel A, Brosh-Nissimov T, Glinert I, et al. Detection and infectivity potential of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) environmental contamination in isolation units and quarantine facilities. *Clinical Microbiology and Infection* 2020; PRE-PROOF.

48. Munoz-Price LS, Rivera F and Ledeboer N. Air contamination of households versus hospital inpatient rooms occupied by SARS-CoV-2 positive patients. *Infect Control Hosp Epidemiol* 2021: 1-14. 2021/02/05. DOI: 10.1017/ice.2021.45.

49. Feng B, Xu K, Gu S, et al. Multi-route transmission potential of SARS-CoV-2 in healthcare facilities. *Journal of Hazardous Materials* 2021; 402.

50. Zhou J, Otter JA, Price JR, et al. Investigating SARS-CoV-2 surface and air contamination in an acute healthcare setting during the peak of the COVID-19 pandemic in London. *medRxiv* 2020; PREPRINT. DOI: **https://doi.org/10.1101/2020.05.24.20110346**.

51. Nissen K, Krambrich J, Akaberi D, et al. Long-distance airborne dispersal of SARS-CoV-2 in COVID-19 wards. *Sci Rep* 2020; 10: 19589. 2020/11/13. DOI: 10.1038/s41598-020-76442-2.

52. Cheng VC, Fung KS, Siu GK, et al. Nosocomial outbreak of COVID-19 by possible airborne transmission leading to a superspreading event. *Clin Infect Dis* 2021 2021/04/15. DOI: 10.1093/cid/ciab313.

53. de Oliveira PM, Mesquita LCC, Gkantonas S, et al. Evolution of spray and aerosol from respiratory releases: theoretical estimates for insight on viral transmission. *Proceedings of the Royal Society A* 2021; 477.

54. Heneghan CJ, Spencer EA, Brassey J, et al. SARS-CoV-2 and the role of airborne transmission: a systematic review [version 1; peer review: 1 approved with reservations, 2 not approved]. *F1000 Research* 2021; 10: 232.

55. Lednicky JA, Lauzardo M, Fan ZH, et al. Viable SARS-CoV-2 in the air of a hospital room with COVID-19 patients. *medRxiv* 2020; PRE-PRINT.

56. Santarpia J, Rivera D, Herrera V, et al. Transmission potential of SARS-CoV-2 in viral shedding observed at the University of Nebraska Medical Centre. *medRxiv* 2020; NOT PEER REVIEWED.

57. Binder RA, Alarja NA, Robie ER, et al. Environmental and Aerosolized SARS-CoV-2 Among Hospitalized COVID-19 Patients. *J Infect Dis* 2020 2020/09/10. DOI: 10.1093/infdis/jiaa575.

58. Tran K, Cimon K, Severn M, et al. Aerosol generating procedures and risk of transmission of acute respiratory infections to healthcare workers: a systematic review. *PLoS One* 2012; 7: e35797. 2012/05/09. DOI: 10.1371/journal.pone.0035797.

59. Heinzerling A, Stuckey MJ, Scheuer T, et al. Transmission of COVID-19 to Health Care Personnel During Exposures to a Hospitalized Patient - Solano County, California, February 2020. *MMWR Morb Mortal Wkly Rep* 2020; 69: 472-476. 2020/04/17. DOI: 10.15585/mmwr.mm6915e5.

60. World Health Organization. Infection prevention and control of epidemic and pandemic prone acute respiratory infections in health care. WHO Guidelines. 2014.

61. Thompson KA, Pappachan JV, Bennett AM, et al. Influenza aerosols in UK hospitals during the H1N1 (2009) pandemic--the risk of aerosol generation during medical procedures. *PLoS One* 2013; 8: e56278. 2013/02/19. DOI: 10.1371/journal.pone.0056278.

62. Chung FF, Lin HL, Liu HE, et al. Aerosol distribution during open suctioning and long-term surveillance of air quality in a respiratory care center within a medical center. *Respir Care* 2015; 60: 30-37. 2014/10/16. DOI: 10.4187/respcare.03310.

63. Simonds AK, Hanak A, Chatwin M, et al. Evaluation of droplet dispersion during non-invasive ventilation, oxygen therapy, nebuliser treatment and chest physiotherapy in clinical practice: implications for management of pandemic influenza and other airborne infections. *Health Technol Assess* 2010; 14: 131-172. 2010/10/07. DOI: 10.3310/hta14460-02.

64. Hamilton F, Gregson F, Arnold D, et al. Aerosol emission from the respiratory tract: an analysis of relative risks from oxygen delivery systems. . *MedRxiv* 2021; PREPRINT.

65. Health Protection Scotland. *Assessing the evidence base for medical procedures which create a higher risk of respiratory infection transmission from patient to healthcare worker.* 12 May 2020 2020.

66. European Centre for Disease Prevention and Control. *Threat assessment brief: rapid increase of a SARS-CoV-2 variant with multiple spike protein mutations observed in the United Kingdom.* 20 December 2020 2020. ECDC.

67. Kidd M, Richter A, Best A, et al. S-variant SARS-CoV-2 is associated with significantly higher viral loads in samples tested by ThermoFisher TaqPath RT-QPCR. *MedRxiv* 2020; NOT PEER REVIEWED.

68. Rogero-Blanco E, Gonzalez-Garcia V, Garcia RM, et al. Characteristics of a COVID-19 confirmed case series in primary care (COVID-19-PC project): a cross-sectional study. *BMC Family Practice* 2021; 22: 66.

69. Gaythorpe K, Imai N, Cuomo-Dannenburg G, et al. *Report 8: Symptom progression of COVID-19*. 11 March 2020 2020. Imperial College London: Imperial College London.

70. Ma S, Zhang J, Zeng M, et al. Epidemiological parameters of coronavirus disease 2019: a pooled analysis of publicly reported individual data of 1155 cases from seven countries. *medRxiv* 2020; NOT PEER REVIEWED.

71. Li W, Zhang B, Lu J, et al. The characteristics of household transmission of COVID-19. *Clin Infect Dis* 2020 2020/04/18. DOI: 10.1093/cid/ciaa450.

72. Wang X, Fang J, Zhu Y, et al. Clinical characteristics of non-critically ill patients with novel coronavirus infection (COVID-19) in a Fangcang Hospital. *Clin Microbiol Infect* 2020 2020/04/07. DOI: 10.1016/j.cmi.2020.03.032.

73. Xu XW, Wu XX, Jiang XG, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. *BMJ (Clinical research ed)* 2020; 368: m606.

74. Wang L, Duan Y, Zhang W, et al. Epidemiologic and Clinical Characteristics of 26 Cases of COVID-19 Arising from Patient-to-Patient Transmission in Liaocheng, China. *Clin Epidemiol* 2020; 12: 387-391. 2020/04/21. DOI: 10.2147/CLEP.S249903.

75. Zheng Y, Xiong C, Liu Y, et al. Epidemiological and clinical characteristics analysis of COVID-19 in the surrounding areas of Wuhan, Hubei Province in 2020. *Pharmacol Res* 2020; 157: 104821. 2020/05/04. DOI: 10.1016/j.phrs.2020.104821.

76. Xia XY, Wu J, Liu HL, et al. Epidemiological and initial clinical characteristics of patients with family aggregation of COVID-19. *J Clin Virol* 2020; 127: 104360. 2020/04/19. DOI: 10.1016/j.jcv.2020.104360.

77. Li Y, Xu S, Du T, et al. Clinical features of 2019 novel coronavirus infection in Beijing. *Journal of Thoracic Disease* 2020; 12: 2563-2568.

78. Liu L, Lei X, Xiao X, et al. Epidemiological and Clinical Characteristics of Patients With Coronavirus Disease-2019 in Shiyan City, China. *Frontiers in Cellular and Infection Microbiology* 2020; 10.

79. Patel NA. Pediatric COVID-19: Systematic review of the literature. *Am J Otolaryngol* 2020; 41: 102573. 2020/06/13. DOI: 10.1016/j.amjoto.2020.102573.

80. Alsofayan YM, Althunayyan SM, Khan AA, et al. Clinical characteristics of COVID-19 in Saudi Arabia: A national retrospective study. *J Infect Public Health* 2020 2020/06/15. DOI: 10.1016/j.jiph.2020.05.026.

81. Salva EP, Villarama JB, Lopez EB, et al. Epidemiological and clinical characteristics of patients with suspected COVID-19 admitted in Metro Manila, Philippines. *Trop Med Health* 2020; 48: 51. 2020/06/25. DOI: 10.1186/s41182-020-00241-8.

82. Alimohamadi YS, Taghdir M and Hosamirudsari H. Determine the most common clinical symptoms in COVID-19 patients: a systematic review and meta-analysis. . *Journal of Preventative Medicine and Hygiene* 2020; 61.

83. Huang J, Li J, Zou Z, et al. Clinical Characteristics of 3 Patients Infected with COVID-19: Age, Interleukin 6 (IL-6), Lymphopenia, and Variations in Chest Computed Tomography (CT). *Am J Case Rep* 2020; 21: e924905. 2020/10/15. DOI: 10.12659/AJCR.924905.

84. Zhang X, Wang H, Wang Y, et al. Epidemiological and clinical based study on four passages of COVID-19 patients: intervention at asymptomatic period contributes to early recovery. *BMC Infect Dis* 2020; 20: 855. 2020/11/19. DOI: 10.1186/s12879-020-05570-x.

85. Lampl BMJ, Buczovsky M, Martin G, et al. Clinical and epidemiological data of COVID-19 from Regensburg, Germany: a retrospective analysis of 1084 consecutive cases. *Infection* 2021: 1-9. 2021/03/06. DOI: 10.1007/s15010-021-01580-2.

86. Zhang H, Du F, Cao XJ, et al. Clinical characteristics of coronavirus disease 2019 (COVID-19) in patients out of Wuhan from China: a case control study. *BMC Infect Dis* 2021; 21: 207. 2021/02/26. DOI: 10.1186/s12879-021-05897-z.

87. Tomlins J, Hamilton F, Gunning S, et al. Clinical features of 95 sequential hospitalised patients with novel coronavirus 2019 disease (COVID-19), the first UK cohort. *J Infect* 2020 2020/05/01. DOI: 10.1016/j.jinf.2020.04.020.

88. ISARIC. ISARIC clinical data report 20 November 2020. *medRxiv* 2020; PRE-PRINT.

89. Millar JE, Neyton L, Seth S, et al. Robust, reproducible clinical patterns in hospitalised patients with COVID-19. *medRxiv* 2020; PRE-PRINT.

90. Clemency BM, Varughese R, Scheafer DK, et al. Symptom Criteria for COVID-19 Testing of Heath Care Workers. *Acad Emerg Med* 2020; 27: 469-474. 2020/05/13. DOI: 10.1111/acem.14009.

91. Chau NVV and al. e. The natural history and transmission potential of asymptomatic SARS-CoV-2 infection. *medRxiv* 2020; PRE-PRINT. DOI: **https://doi.org/10.1101/2020.04.27.20082347**.

92. Paoli D, Pallotti F, Colangelo S, et al. Study of SARS-CoV-2 in semen and urine samples of a volunteer with positive naso-pharyngeal swab. *J Endocrinol Invest* 2020 2020/04/25. DOI: 10.1007/s40618-020-01261-1.

93. Altin F, Cingi C, Uzun T, et al. Olfactory and gustatory abnormalities in COVID-19 cases. *Eur Arch Otorhinolaryngol* 2020 2020/06/25. DOI: 10.1007/s00405-020-06155-9.

94. Noh JY, Yoon JG, Seong H, et al. Asymptomatic infection and atypical manifestations of COVID-19: Comparison of viral shedding duration. *J Infect* 2020 2020/05/24. DOI: 10.1016/j.jinf.2020.05.035.

95. Viner R, Ward J, Hudson L, et al. Systematic review of reviews of symptoms and signs of COVID-19 in children and adolescents. MedRxiv 2020; NOT PEER REVIEWED.

96. Maltezou HC, Magaziotou I, Dedoukou X, et al. Children and Adolescents With SARS-CoV-2 Infection: Epidemiology, Clinical Course and Viral Loads. Pediatr Infect Dis J 2020 2020/10/09. DOI: 10.1097/INF.0000000000002899.

97. CDC COVID-19 Response Team. Coronavirus diseaes 2019 in children - United States, February 12 - April 2, 2020. Morbidity and Mortality Weekly Report 2020; 69: 422-426.

98. Tan YP, Tan BY, Pan J, et al. Epidemiologic and clinical characteristics of 10 children with coronavirus disease 2019 in Changsha, China. J Clin Virol 2020; 127: 104353. 2020/04/18. DOI: 10.1016/j.jcv.2020.104353.

99. Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. Acta Paediatr 2020; 109: 1088-1095. 2020/03/24. DOI: 10.1111/apa.15270.

100. Chang TH, Wu JL and Chang LY. Clinical characteristics and diagnostic challenges of pediatric COVID-19: A systematic review and meta-analysis. J Formos Med Assoc 2020; 119: 982-989. 2020/04/21. DOI: 10.1016/j.jfma.2020.04.007.

101. Zhen-Dong Y, Gao-Jun Z, Run-Ming J, et al. Clinical and transmission dynamics characteristics of 406 children with coronavirus disease 2019 in China: A review. J Infect 2020 2020/05/04. DOI: 10.1016/j.jinf.2020.04.030.

102. Dong Y, Mo X, Hu Y, et al. Epidemiology of COVID-19 Among Children in China. Pediatrics 2020; 145 2020/03/18. DOI: 10.1542/peds.2020-0702.

103. Swann OV, Holden KA, Turtle L, et al. Clinical characteristics of children and young people admitted to hospital with COVID-19 in United Kingdom: prospective multicentre observational cohort study. British Medical Journal 2020; Pre-print.

104. Heudorf U, Steul K and Gottschalk R. Sars-Cov-2 in children - insights and conclusions from the mandatory reporting data in Frankfurt am Main, Germany, March-July 2020. GMS Hyg Infect Control 2020; 15: Doc24. 2020/11/21. DOI: 10.3205/dgkh000359.

105. Graham NSN, Junghans C, Downes R, et al. SARS-CoV-2 infection, clinical features and outcome of COVID-19 in United Kingdom nursing homes. medRxiv 2020; PRE-PRINT. DOI: https://doi.org/10.1101/2020.05.19.20105460.

106. Zuin M, Rigatelli G, Zuliani G, et al. Arterial hypertension and risk of death in patients with COVID-19 infection: Systematic review and meta-analysis. J Infect 2020 2020/04/14. DOI: 10.1016/j.jinf.2020.03.059.

107. CDC COVID-19 Response Team. Preliminary Estimates of the Prevalence of Selected Underlying Health Conditions Among Patients with Coronavirus Disease 2019 — United States, February 12–March 28, 2020. Morbidity and Mortality Weekly Report 2020; 69.

108. Lian J, Jin X, Hao S, et al. Epidemiological, clinical, and virological characteristics of 465 hospitalized cases of coronavirus disease 2019 (COVID-19) from Zhejiang province in China. Influenza Other Respir Viruses 2020 2020/05/13. DOI: 10.1111/irv.12758.

109. Khan MA, Khan N, Mustagir G, et al. Effects of pre-existing morbidities on occurrence of death among COVID-19 disease patients: A systematic review and meta-analysis. MedRxiv 2020; PRE-PRINT.

110. Rogado J, Obispo B, Pangua C, et al. Covid-19 transmission, outcome and associated risk factors in cancer patients at the first month of the pandemic in a Spanish hospital in Madrid. Clin Transl Oncol 2020 2020/05/26. DOI: 10.1007/s12094-020-02381-z.

111. Thompson CN, Baumgartner J, Pichardo C, et al. COVID-19 Outbreak - New York City, February 29-June 1, 2020. MMWR Morb Mortal Wkly Rep 2020; 69: 1725-1729. 2020/11/20. DOI: 10.15585/mmwr.mm6946a2.

112. CDC. Science Brief: Evidence used to update the list of underlying medical conditions that increase a person's risk of severe illness from COVID-19. 2021.

113. Field RE, Afzal I, Dixon J, et al. Cohort profile: Preliminary experience of 500 COVID-19 positive cases at a

South West London District General Hospital. medRxiv 2020; UNPUBLISHED. DOI: https://doi.org/10.1101/2020.04.28.20075119.

114. Mannheim J, Gretsch S, Layden JE, et al. Characteristics of Hospitalized Pediatric COVID-19 Cases - Chicago, Illinois, March - April 2020. J Pediatric Infect Dis Soc 2020 2020/06/02. DOI: 10.1093/jpids/piaa070.

115. Zhao X. ZB, Li P., Ma C., Gu J., Hou P., Gou Z., Wu H., Bai Y. Incidence, clinical characteristics and prognostic factors of patients with COVID-19: a systematic review and meta-analysis. medRxiv 2020.

116. Chu J, Yang N, Wei Y, et al. Clinical characteristics of 54 medical staff with COVID-19: A retrospective study in a single center in Wuhan, China. J Med Virol 2020 2020/03/31. DOI: 10.1002/jmv.25793.

117. Tian Y, Rong L, Nian W, et al. Review article: gastrointestinal features in COVID-19 and the possibility of faecal transmission. Aliment Pharmacol Ther 2020; 51: 843-851. 2020/03/31. DOI: 10.1111/apt.15731.

118. Lee IC, Huo TI and Huang YH. Gastrointestinal and Liver Manifestations in Patients with COVID-19. J Chin Med Assoc 2020 2020/04/04. DOI: 10.1097/JCMA.0000000000000319.

119. Chen Y, Chen L, Deng Q, et al. The Presence of SARS-CoV-2 RNA in Feces of COVID-19 Patients. J Med Virol 2020 2020/04/04. DOI: 10.1002/jmv.25825.

120. Zhang R, Ouyang H, Fu L, et al. CT features of SARS-CoV-2 pneumonia according to clinical presentation: a retrospective analysis of 120 consecutive patients from Wuhan city. Eur Radiol 2020 2020/04/13. DOI: 10.1007/s00330-020-06854-1.

121. D'Amico F, Baumgart DC, Danese S, et al. Diarrhea during COVID-19 infection: pathogenesis, epidemiology, prevention and management. Clin Gastroenterol Hepatol 2020 2020/04/12. DOI: 10.1016/j.cgh.2020.04.001.

122. Liu J, Liao X, Qian S, et al. Community Transmission of Severe Acute Respiratory Syndrome Coronavirus 2, Shenzhen, China, 2020. Emerging Infectious Diseases 2020; 26: 17.

123. Cheung KS, Hung IFN, Chan PPY, et al. Gastrointestinal Manifestations of SARS-CoV-2 Infection and Virus Load in Fecal Samples From a Hong Kong Cohort: Systematic Review and Meta-analysis. Gastroenterology 2020 2020/04/07. DOI: 10.1053/j.gastro.2020.03.065.

124. An P, Chen H, Ren H, et al. Gastrointestinal Symptoms Onset in COVID-19 Patients in Wuhan, China. Dig Dis Sci 2020 2020/11/13. DOI: 10.1007/s10620-020-06693-6.

125. Comoglu S, Ozturk S, Kant A, et al. Evaluation of Diarrhea in Patients with COVID-19. Digestive Diseases 2021; 01: 01.

126. Leal T, Costa E, Arroja B, et al. Gastrointestinal manifestations of COVID-19: results from a European centre. European Journal of Gastroenterology & Hepatology 2021; 33: 691-694.

127. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med 2020 2020/02/29. DOI: 10.1056/NEJMoa2002032.

128. Gao QY, Chen YX and Fang JY. 2019 novel coronavirus infection and gastrointestinal tract. Journal of digestive diseases 2020; 25.

129. Yeo C, Kaushal S and Yeo D. Enteric involvement of coronaviruses: is faecal-oral transmission of SARS-CoV-2 possible? The lancet Gastroenterology & hepatology 2020; 19.

130. Tang A TZ-d, Wang H-l, Dai Y-x, Li K-f, Liu J-n, et al. . Detection of novel coronavirus by RT-PCR in stool specimen from asymptomatic child, China. . Emerging Infectious Diseases 2020; 26.

131. Holshue ML, DeBolt C, Lindquist S, et al. First Case of 2019 Novel Coronavirus in the United States. N Engl J Med 2020; 382: 929-936. 2020/02/01. DOI: 10.1056/NEJMoa2001191.

132. Zhang W, Du RH, Li B, et al. Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. Emerg Microbes Infect 2020; 9: 386-389. 2020/02/18. DOI: 10.1080/22221751.2020.1729071.

133. Young Park J. SHM, Un Park K., Young Kim J., Hwa Choi E. First pediatric case of coronavirus disease 2019 in Korea. Journal of Korean Medical Science 2020; 35.

134. Zhang T, Cui X, Zhao X, et al. Detectable SARS-CoV-2 viral RNA in feces of three children during recovery period of COVID-19 pneumonia. J Med Virol 2020 2020/03/31. DOI: 10.1002/jmv.25795.

135. Xiao F, Tang M, Zheng X, et al. Evidence for Gastrointestinal Infection of SARS-CoV-2. Gastroenterology 2020 2020/03/07. DOI: 10.1053/j.gastro.2020.02.055.

136. Nicastri E, D'Abramo A, Faggioni G, et al. Coronavirus disease (COVID-19) in a paucisymptomatic patient: epidemiological and clinical challenge in settings with limited community transmission, Italy, February 2020. Euro Surveill 2020; 25 2020/03/27. DOI: 10.2807/1560-7917.ES.2020.25.11.2000230.

137. Novazzi F, Cassaniti I, Piralla A, et al. SARS-CoV-2 positivity in rectal swabs implication for possible transmission. Journal of Global Antimicrobial Resistance 2020. DOI: https://doi.org/10.1016/j.jgar.2020.06.011.

138. Wong MC, Huang J, Lai C, et al. Detection of SARS-CoV-2 RNA in fecal specimens of patients with confirmed COVID-19: A meta-analysis. J Infect 2020 2020/06/15. DOI: 10.1016/j.jinf.2020.06.012.

139. van Doorn AS, Meijer B, Frampton CMA, et al. Systematic review with meta-analysis: SARS-CoV-2 stool testing and the potential for faecal-oral transmission. Aliment Pharmacol Ther 2020 2020/08/28. DOI: 10.1111/apt.16036.

140. Cuicchi D, Lazzarotto T and Poggioli G. Fecal-oral transmission of SARS-CoV-2: review of laboratory-confirmed virus in gastrointestinal system. Int J Colorectal Dis 2020 2020/10/16. DOI: 10.1007/s00384-020-03785-7.

141. Santos VS, Gurgel RQ, Cuevas LE, et al. Prolonged fecal shedding of SARS-CoV-2 in pediatric patients. A quantitative evidence synthesis. J Pediatr Gastroenterol Nutr 2020 2020/05/27. DOI: 10.1097/MPG.0000000000002798.

142. Cho SM and Ha GY. A Case of COVID-19 in a 45-Day-Old Infant with Persistent Fecal Virus Shedding for More Than 12 Weeks. Yonsei Med J 2020; 61: 901-903. 2020/09/26. DOI: 10.3349/ymj.2020.61.10.901.

143. Prakash S, Shukla S, Mishra H, et al. SARS-CoV-2 -RNA persists longer in faecal sample as compared to nasal and throat swab samples of COVID-19 patients'; an observational study. *Indian journal of medical microbiology* 2021; 39: 122-124.

144. Li J, Feng J, Liu TH, et al. An infant with a mild SARS-CoV-2 infection detected only by anal swabs: a case report. *Braz J Infect Dis* 2020 2020/05/12. DOI: 10.1016/j.bjid.2020.04.009.

145. Xu Y, Li X, Zhu B, et al. Characteristics of pediatric SARS-CoV-2 infection and potential evidence for persistent fecal viral shedding. *Nat Med* 2020; 26: 502-505. 2020/04/15. DOI: 10.1038/s41591-020-0817-4.

146. Park SK, Lee CW, Park DI, et al. Detection of SARS-CoV-2 in Fecal Samples from Patients with Asymptomatic and Mild COVID-19 in Korea. *Clin Gastroenterol Hepatol* 2020 2020/06/14. DOI: 10.1016/j.cgh.2020.06.005.

147. Shaban RZ, Li C, O'Sullivan MVN, et al. COVID-19 in Australia: Our national response to the first cases of SARS-CoV-2 infection during the early biocontainment phase. *Intern Med J* 2020 2020/11/17. DOI: 10.1111/imj.15105.

148. Morone G, Palomba A, Iosa M, et al. Incidence and Persistence of Viral Shedding in COVID-19 Post-acute Patients With Negativized Pharyngeal Swab: A Systematic Review. *Front Med (Lausanne)* 2020; 7: 562. 2020/09/29. DOI: 10.3389/fmed.2020.00562.

149. Wolfel R, Corman V.M., Guggemos W., Seilmaier M., Zange S., Muller M.A., Niemeyer D., Jones Kelly T.C., Vollmar P., Rothe C., Hoelscher M., Bleicker T., Brunink S., Schneider J., Ethmann R.., Zwirglmaeier K., Drosten C., Wendtner C. Virological assessment of hospitalized cases of coronavirus disease 2019. *medRxiv* 2020.

150. Xiao F, Sun J, Xu Y, et al. Infectious SARS-CoV-2 in Feces of Patient with Severe COVID-19. *Emerg Infect Dis* 2020; 26 2020/05/19. DOI: 10.3201/eid2608.200681.

151. van Kampen JJA and al. e. Shedding of infectious virus in hospitalised patients with coronavirus disease-2019 (COVID-19): duration and key determinants. *medRxiv* 2020; PREPRINT. DOI: **https://doi.org/10.1101/2020.06.08.20125310**.

152. Chan JFW, Yuan S, Kok KH, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *The Lancet* 2020; 395: 514-523.

153. Chang L, Zhao L, Gong H, et al. Severe acute respiratory syndrome coronavirus 2 RNA detected in blood donations. *Emerging infectious diseases* 2020; 26.

154. Peng L, Liu J, Xu W, et al. 2019 novel coronavirus can be detected in urine, blood, anal swabs and oropharyngeal swabs samples. *medRxiv* 2020; NOT PEER REVIEWED.

155. Han MS, Seong MW, Kim N, et al. Viral RNA Load in Mildly Symptomatic and Asymptomatic Children with COVID-19, Seoul. *Emerg Infect Dis* 2020; 26 2020/06/05. DOI: 10.3201/eid2610.202449.

156. Kim JM, Kim HM, Lee EJ, et al. Detection and Isolation of SARS-CoV-2 in Serum, Urine, and Stool Specimens of COVID-19 Patients from the Republic of Korea. *Osong Public Health Res Perspect* 2020; 11: 112-117. 2020/06/13. DOI: 10.24171/j.phrp.2020.11.3.02.

157. Fajnzylber J, Regan J, Coxen K, et al. SARS-CoV-2 viral load is associated with increased disease severity and mortality. *Nat Commun* 2020; 11: 5493. 2020/11/01. DOI: 10.1038/s41467-020-19057-5.

158. Chaves DG, da Silva Malta MCF, de Souza Madeira Ferreira Boy L, et al. Analysis of current SARS-CoV-2 infection in a large population of blood donors evidenced that RNAemia is rare in plasma. *Transfusion* 2021; 16: 16.

159. Schwartz A, Yogev Y, Zilberman A, et al. Detection of SARS-CoV-2 in vaginal swabs of women with acute SARS-CoV-2 infection: a prospective study. *BJOG* 2020 2020/10/07. DOI: 10.1111/1471-0528.16556.

160. Qiu L, Liu X, Xiao M, et al. SARS-CoV-2 is not detectable in the vaginal fluid of women with severe COVID-19 infection. *Clin Infect Dis* 2020 2020/04/03. DOI: 10.1093/cid/ciaa375.

161. Khoiwal K, Kalita D, Shankar R, et al. Identification of SARS-CoV-2 in the vaginal fluid and cervical exfoliated cells of women with active COVID-19 infection: A pilot study. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics* 2021; 13.

162. Demirel C, Tulek F, Celik HG, et al. Failure to Detect Viral RNA in Follicular Fluid Aspirates from a SARS-CoV-2-Positive Woman. *Reprod Sci* 2021 2021/02/23. DOI: 10.1007/s43032-021-00502-9.

163. Song C, Wang Y, Li W, et al. Absence of 2019 Novel Coronavirus in Semen and Testes of COVID-19 Patients. *Biol Reprod* 2020 2020/04/17. DOI: 10.1093/biolre/ioaa050.

164. Zhang S, Wang X, Zhang H, et al. The absence of coronavirus in expressed prostatic secretion in COVID-19 patients in Wuhan city. *Reprod Toxicol* 2020; 96: 90-94. 2020/06/14. DOI: 10.1016/j.reprotox.2020.06.006.

165. Li D, Jin M, Bao P, et al. Clinical Characteristics and Results of Semen Tests Among Men With Coronavirus Disease 2019. *JAMA Netw Open* 2020; 3: e208292. 2020/05/08. DOI: 10.1001/jamanetworkopen.2020.8292.

166. Gacci M, Coppi M, Baldi E, et al. Semen impairment and occurrence of SARS-CoV-2 virus in semen after recovery from COVID-19. *Hum Reprod* 2021 2021/02/02. DOI: 10.1093/humrep/deab026.

167. Pan F, Xiao X, Guo J, et al. No evidence of severe acute respiratory syndrome-coronavirus 2 in semen of males recovering from coronavirus disease 2019. *Fertil Steril* 2020; 113: 1135-1139. 2020/06/03. DOI: 10.1016/j.fertnstert.2020.04.024.

168. Holtmann N, Edimiris P, Andree M, et al. Assessment of SARS-CoV-2 in human semen-a cohort study. *Fertil Steril* 2020 2020/07/12. DOI: 10.1016/j.fertnstert.2020.05.028.

169. Rawlings SA, Ignacio C, Porrachia M, et al. No Evidence of SARS-CoV-2 Seminal Shedding Despite SARS-CoV-2 Persistence in the Upper Respiratory Tract. *Open Forum Infect Dis* 2020; 7: ofaa325. 2020/09/03. DOI: 10.1093/ofid/ofaa325.

170. Sun J, Zhu A, Li H, et al. Isolation of Infectious SARS-CoV-2 from Urine of a COVID-19 Patient. *Emerg Microbes Infect* 2020: 1-8. 2020/04/29. DOI: 10.1080/22221751.2020.1760144.

171. Nomoto H, Ishikane M, Katagiri D, et al. Cautious handling of urine from moderate to severe COVID-19 patients. *Am J Infect Control* 2020; 48: 969-971. 2020/06/06. DOI: 10.1016/j.ajic.2020.05.034.

172. Mattos EC, Matsuda EM, Colpas DR, et al. Can urine be a potential biohazard in times of SARS-CoV-2 pandemic? *J Med Virol* 2020 2020/10/22. DOI: 10.1002/jmv.26616.

173. Kashi AH, De la Rosette J, Amini E, et al. Urinary Viral Shedding of COVID-19 and its Clinical Associations: A Systematic Review and Meta-analysis of Observational Studies. *Urol J* 2020 2020/09/06. DOI: 10.22037/uj.v16i7.6248.

174. Jones D, Faluyi D, Hamilton S, et al. A Prospective Study to Identify Rates of SARS-CoV-2 Virus in the Peritoneum and Lower Genital Tract of Patients Having Surgery: An Observational Study. *Journal of Minimally Invasive Gynecology* 2021.

175. Ngaserin SH, Koh FH, Ong BC, et al. COVID-19 not detected in peritoneal fluid: a case of laparoscopic appendicectomy for acute appendicitis in a COVID-19-infected patient. *Langenbecks Arch Surg* 2020; 405: 353-355. 2020/05/10. DOI: 10.1007/s00423-020-01891-2.

176. Matuck BF, Dolhnikoff M, Maia GVA, et al. Periodontal tissues are targets for SARS-CoV-2: a post-mortem study. *Journal of Oral Microbiology* 2020; 13.

177. Wu P, Duan F, Luo C, et al. Characteristics of Ocular Findings of Patients With Coronavirus Disease 2019 (COVID-19) in Hubei Province, China. *JAMA Ophthalmol* 2020 2020/04/02. DOI: 10.1001/jamaophthalmol.2020.1291.

178. Zhang X, Chen X, Chen L, et al. The evidence of SARS-CoV-2 infection on ocular surface. *Ocul Surf* 2020 2020/04/15. DOI: 10.1016/j.jtos.2020.03.010.

179. Salducci M and La Torre G. COVID-19 emergency in the cruise's ship: a case report of conjunctivitis. *Clin Ter* 2020; 171: e189-e191. 2020/04/24. DOI: 10.7417/CT.2020.2212.

180. Karimi S, Arabi A, Shahraki T, et al. Detection of severe acute respiratory syndrome Coronavirus-2 in the tears of patients with Coronavirus disease 2019. *Eye (Lond)* 2020 2020/05/20. DOI: 10.1038/s41433-020-0965-2.

181. Liang L and Wu P. There may be virus in conjunctival secretion of patients with COVID-19. *Acta Ophthalmol* 2020; 98: 223. 2020/03/20. DOI: 10.1111/aos.14413.

182. Valente P, Iarossi G, Federici M, et al. Ocular manifestations and viral shedding in tears of pediatric patients with coronavirus disease 2019: a preliminary report. *J AAPOS* 2020 2020/06/13. DOI: 10.1016/j.jaapos.2020.05.002.

183. Colavita F, Lapa D, Carletti F, et al. Virological characterization of the first 2 COVID-19 patients diagnosed in Italy: phylogenetic analysis, virus shedding profile from different body sites, and antibody response kinetics. . 2020; Open Forum Infectious Diseases.

184. Hu Y, Chen T, Liu M, et al. Positive detection of SARS-CoV-2 combined HSV1 and HHV6B virus nucleic acid in tear and conjunctival secretions of a non-conjunctivitis COVID-19 patient with obstruction of common lacrimal duct. *Acta Ophthalmol* 2020 2020/05/15. DOI: 10.1111/aos.14456.

185. Fang Z, Zhang Y, Hang C, et al. Comparisons of viral shedding time of SARS-CoV-2 of different samples in ICU and non-ICU patients. *J Infect* 2020; 81: 147-178. 2020/03/27. DOI: 10.1016/j.jinf.2020.03.013.

186. Arora R, Goel R, Kumar S, et al. Evaluation of SARS-CoV-2 in tears of moderate to severe COVID-19 patients. *Ophthalmology* 2020 2020/09/04. DOI: 10.1016/j.ophtha.2020.08.029.

187. Hanege FM, Kocoglu E, Kalcioglu MT, et al. SARS-CoV-2 presence in the saliva, tears and cerumen of COVID-19 patients. *Laryngoscope* 2020 2020/10/24. DOI: 10.1002/lary.29218.

188. Li M, Yang Y, He T, et al. Detection of SARS-CoV-2 in the ocular surface in different phases of COVID-19 patients in Shanghai, China. *Ann Transl Med* 2021; 9: 100. 2021/02/12. DOI: 10.21037/atm-20-6026.

189. Li JPO, Lam DSC, Chen Y, et al. Novel Coronavirus disease 2019 (COVID-19): The importance of recognising possible early ocular manifestation and using protective eyewear. *The British journal of ophthalmology* 2020; 104: 297-298. Editorial.

190. Lu CW, Liu XF and Jia ZF. 2019-nCoV transmission through the ocular surface must not be ignored. *The Lancet* 2020; 395: e39. Letter.

191. Liu S, Yeung TLM, Tso EYK, et al. Study of conjunctival carriage of SARS-CoV-2 using serial sampling: risk factors and protective factors. *Can J Ophthalmol* 2021 2021/02/01. DOI: 10.1016/j.jcjo.2021.01.003.

192. Charki S, Gamini BS, Biradar V, et al. Experience of covid-19 infections in neonates in tertiary care centre in North Karnataka, India: A prospective cohort study. *Current Pediatric Research* 2021; 25: 421-425.

193. Blasco Santana L, Miraval Wong E, Alvarez-Troncoso J, et al. Maternal and perinatal outcomes and placental pathologic examination of 29 SARS-CoV-2 infected patients in the third trimester of gestation. *Journal of Obstetrics & Gynaecology Research* 2021; 05: 05.

194. Chen H, Guo J, Wang C, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *The Lancet* 2020.

195. Yu N, Li W, Kang Q, et al. Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-centre, descriptive study. *Lancet Infect Dis* 2020 2020/03/30. DOI: 10.1016/S1473-3099(20)30176-6.

196. Yang P, Wang X, Liu P, et al. Clinical characteristics and risk assessment of newborns born to mothers with COVID-19. *J Clin Virol* 2020; 127: 104356. 2020/04/18. DOI: 10.1016/j.jcv.2020.104356.

197. Chen Y, Peng H, Wang L, et al. Infants Born to Mothers With a New Coronavirus (COVID-19). *Front Pediatr* 2020; 8: 104. 2020/04/09. DOI: 10.3389/fped.2020.00104.

198. Lu D, Sang L, Du S, et al. Asymptomatic COVID-19 infection in late pregnancy indicated no vertical transmission. *J Med Virol* 2020 2020/04/25. DOI: 10.1002/jmv.25927.

199. Kuhrt K, McMicking J, Nanda S, et al. Placental abruption in a twin pregnancy at 32 weeks' gestation complicated by COVID-19, without vertical transmission to the babies. *Am J Obstet Gynecol MFM* 2020: 100135. 2020/05/12. DOI: 10.1016/j.ajogmf.2020.100135.

200. Lyra J, Valente R, Rosario M, et al. Cesarean Section in a Pregnant Woman with COVID-19: First Case in Portugal. *Acta Med Port* 2020; 33: 429-431. 2020/05/01. DOI: 10.20344/amp.13883.

201. Sun M, Xu G, Yang Y, et al. Evidence of mother-to-newborn infection with COVID-19. *Br J Anaesth* 2020 2020/05/11. DOI: 10.1016/j.bja.2020.04.066.

202. Prabhu M, Cagino K, Matthews KC, et al. Pregnancy and postpartum outcomes in a universally tested population for SARS-CoV-2 in New York City: A prospective cohort study. *BJOG* 2020 2020/07/08. DOI: 10.1111/1471-0528.16403.

203. Barbero P, Muguerza L, Herraiz I, et al. SARS-CoV-2 in pregnancy: characteristics and outcomes of hospitalized and non-hospitalized women due to COVID-19. *J Matern Fetal Neonatal Med* 2020: 1-7. 2020/07/22. DOI: 10.1080/14767058.2020.1793320.

204. Yan J, Guo J, Fan C, et al. Coronavirus disease 2019 in pregnant women: a report based on 116 cases. *Am J Obstet Gynecol* 2020; 223: 111 e111-111 e114. 2020/04/27. DOI: 10.1016/j.ajog.2020.04.014.

205. Di Mascio D and COVID Wwgo. Maternal and Perinatal Outcomes of Pregnant Women with SARS-COV-2 infection. *Ultrasound Obstet Gynecol* 2020 2020/09/15. DOI: 10.1002/uog.23107.

206. Douglass KM, Strobel KM, Richley M, et al. Maternal-Neonatal Dyad Outcomes of Maternal COVID-19 Requiring Extracorporeal Membrane Support: A Case Series. *Am J Perinatol* 2020 2020/10/18. DOI: 10.1055/s-0040-1718694.

207. Biasucci G, Cannalire G, Raymond A, et al. Safe Perinatal Management of Neonates Born to SARS-CoV-2 Positive Mothers at the Epicenter of the Italian Epidemic. *Front Pediatr* 2020; 8: 565522. 2020/11/17. DOI: 10.3389/fped.2020.565522.

208. Shmakov RG, Prikhodko A, Polushkina E, et al. Clinical course of novel COVID-19 infection in pregnant women. *J Matern Fetal Neonatal Med* 2020: 1-7. 2020/12/01. DOI: 10.1080/14767058.2020.1850683.

209. He Z, Fang Y, Zuo Q, et al. Vertical transmission and kidney damage in newborns from coronavirus disease 2019 infection pregnant mother. *Int J Antimicrob Agents* 2020: 106260. 2020/12/15. DOI: 10.1016/j.ijantimicag.2020.106260.

210. Gao L, Ren J, Xu L, et al. Placental pathology of the third trimester pregnant women from COVID-19. *Diagn Pathol* 2021; 16: 8. 2021/01/15. DOI: 10.1186/s13000-021-01067-6.

211. Zhu H, Wang L, Fang C, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *Transl Pediatr* 2020; 9: 51-60. 2020/03/11. DOI: 10.21037/tp.2020.02.06.

212. de Vasconcelos Gaspar A and Santos Silva I. SARS-CoV-2 in Pregnancy—The First Wave. *Medicina* 2021; 57. DOI: 10.3390/medicina57030241.

213. Oncel MY AI, Kanburoglu MK, Tayman C, Coskun S, Narter F, Er I, Oncan TG, Memisoglu A, Cetinkaya M, Oguz D. A multicenter study on epidemiological and clinical characteristics of 125 newborns born to women infected with COVID-19 by Turkish Neonatal Society. *European Journal of Pediatrics* 2021; 180: 733-742. DOI: **https://doi.org/10.1007/s00431-020-03767-5**.

214. Khan S, Peng L, Siddique R, et al. Impact of COVID-19 infection on pregnancy outcomes and the risk of maternal-to-neonatal intrapartum transmission of COVID-19 during natural birth. *Infect Control Hosp Epidemiol* 2020: 1-3. 2020/04/14. DOI: 10.1017/ice.2020.84.

215. Dong L, Tian J, He S, et al. Possible Vertical Transmission of SARS-CoV-2 From an Infected Mother to Her Newborn. *JAMA* 2020 2020/03/28. DOI: 10.1001/jama.2020.4621.

216. Xiong X, Wei H, Zhang Z, et al. Vaginal Delivery Report of a Healthy Neonate Born to a Convalescent Mother with COVID-19. *J Med Virol* 2020 2020/04/11. DOI: 10.1002/jmv.25857.

217. Liu W, Wang J, Li W, et al. Clinical characteristics of 19 neonates born to mothers with COVID-19. *Front Med* 2020 2020/04/15. DOI: 10.1007/s11684-020-0772-y.

218. Cao D, Yin H, Chen J, et al. Clinical analysis of ten pregnant women with COVID-19 in Wuhan, China: A retrospective study. *Int J Infect Dis* 2020; 95: 294-300. 2020/04/27. DOI: 10.1016/j.ijid.2020.04.047.

219. Penfield CA, Brubaker SG, Limaye MA, et al. Detection of SARS-COV-2 in Placental and Fetal Membrane Samples. *Am J Obstet Gynecol MFM* 2020: 100133. 2020/05/12. DOI: 10.1016/j.ajogmf.2020.100133.

220. De Socio GV, Malincarne L, Arena S, et al. Delivery in Asymptomatic Italian Woman with SARS-CoV-2 Infection. *Mediterr J Hematol Infect Dis* 2020; 12: e2020033. 2020/05/13. DOI: 10.4084/MJHID.2020.033.

221. Perrone S, Deolmi M, Giordano M, et al. Report of a series of healthy term newborns from convalescent mothers with COVID-19. *Acta Biomed* 2020; 91: 251-255. 2020/05/19. DOI: 10.23750/abm.v91i2.9743.

222. Polonia-Valente R, Moucho M, Tavares M, et al. Vaginal delivery in a woman infected with SARS-CoV-2 - The first case reported in Portugal. *Eur J Obstet Gynecol Reprod Biol* 2020; 250: 253-254. 2020/05/23. DOI: 10.1016/j.ejogrb.2020.05.007.

223. Dumitriu D, Emeruwa UN, Hanft E, et al. Outcomes of Neonates Born to Mothers With Severe Acute Respiratory Syndrome Coronavirus 2 Infection at a Large Medical Center in New York City. *JAMA Pediatr* 2020 2020/10/13. DOI: 10.1001/jamapediatrics.2020.4298.

224. Mejía Jiménez I, Salvador López R, García Rosas E, et al. Umbilical cord clamping and skin-to-skin contact in deliveries from women positive for SARS-CoV-2: a prospective observational study. *British Journal of Obstetrics and Gynaecology* 2020; PRE-PRINT.

225. Ronchi A, Pietrasanta C, Zavattoni M, et al. Evaluation of Rooming-in Practice for Neonates Born to Mothers With Severe Acute Respiratory Syndrome Coronavirus 2 Infection in Italy. *JAMA Pediatr* 2020 2020/12/08. DOI: 10.1001/jamapediatrics.2020.5086.

226. Edlow AG, Li JZ, Collier AY, et al. Assessment of Maternal and Neonatal SARS-CoV-2 Viral Load, Transplacental Antibody Transfer, and Placental Pathology in Pregnancies During the COVID-19 Pandemic. *JAMA Netw Open* 2020; 3: e2030455. 2020/12/23. DOI: 10.1001/jamanetworkopen.2020.30455.

227. Solis-Garcia G, Gutierrez-Velez A, Pescador Chamorro I, et al. Epidemiology, management and risk of SARS-CoV-2 transmission in a cohort of newborns born to mothers diagnosed with COVID-19 infection. *An Pediatr (Engl Ed)* 2021 2021/02/02. DOI: 10.1016/j.anpede.2020.12.006.

228. Jani S, Jacques SM, Qureshi F, et al. Clinical Characteristics of Mother-Infant Dyad and Placental Pathology in COVID-19 Cases in Predominantly African American Population. *AJP Rep* 2021; 11: e15-e20. 2021/02/06. DOI: 10.1055/s-0040-1721673.

229. Parazzini F, Bortolus R, Mauri PA, et al. Delivery in pregnant women infected with SARS-CoV-2: A fast review. *Int J Gynaecol Obstet* 2020 2020/04/10. DOI: 10.1002/ijgo.13166.

230. Karimi-Zarchi M, Neamatzadeh H, Dastgheib SA, et al. Vertical Transmission of Coronavirus Disease 19 (COVID-19) from Infected Pregnant Mothers to Neonates: A Review. *Fetal Pediatr Pathol* 2020: 1-5. 2020/04/03. DOI: 10.1080/15513815.2020.1747120.

231. Di Mascio D, Khalil A, Saccone G, et al. Outcome of Coronavirus spectrum infections (SARS, MERS, COVID 1 -19) during pregnancy: a systematic review and meta-analysis. *Am J Obstet Gynecol MFM* 2020: 100107. 2020/04/16. DOI: 10.1016/j.ajogmf.2020.100107.

232. Cheruiyot I, Henry BM and Lippi G. Is there evidence of intra-uterine vertical transmission potential of COVID-19 infection in samples tested by quantitative RT-PCR? *Eur J Obstet Gynecol Reprod Biol* 2020 2020/04/28. DOI: 10.1016/j.ejogrb.2020.04.034.

233. Smith V, Seo D, Warty R, et al. Maternal and neonatal outcomes associated with COVID-19 infection: A systematic review. *PLoS One* 2020; 15: e0234187. 2020/06/05. DOI: 10.1371/journal.pone.0234187.

234. Huntley BJF, Huntley ES, Di Mascio D, et al. Rates of Maternal and Perinatal Mortality and Vertical Transmission in Pregnancies Complicated by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-Co-V-2) Infection: A Systematic Review. *Obstet Gynecol* 2020 2020/06/10. DOI: 10.1097/AOG.0000000000004010.

235. Yuan J, Qian H, Cao S, et al. Is there possibility of vertical transmission of COVID-19: a systematic review. *Translational Pediatrics* 2021; 10: 423-434. Review.

236. Kotlyar A, Grechukhina O, Chen A, et al. Vertical Transmission of COVID-19: A Systematic Review and Meta-analysis. *Am J Obstet Gynecol* 2020 2020/08/03. DOI: 10.1016/j.ajog.2020.07.049.

237. World Health Organization. *World Health Organization, Definition and categorization of the timing of mother-to-child transmission of SARS-CoV-2 - Scientific brief*. 9th February 2021 2021.

238. Zamaniyan M, Ebadi A, Aghajanpoor Mir S, et al. Preterm delivery in pregnant woman with critical COVID-19 pneumonia and vertical transmission. *Prenat Diagn* 2020 2020/04/19. DOI: 10.1002/pd.5713.

239. Patane L, Morotti D, Giunta MR, et al. Vertical transmission of COVID-19: SARS-CoV-2 RNA on the fetal side of the placenta in pregnancies with COVID-19 positive mothers and neonates at birth. *Am J Obstet Gynecol MFM* 2020: 100145. 2020/05/20. DOI: 10.1016/j.ajogmf.2020.100145.

240. Kulkarni R, Rajput U, Dawre R, et al. Early-onset symptomatic neonatal COVID-19 infection with high probability of vertical transmission. *Infection* 2020 2020/08/04. DOI: 10.1007/s15010-020-01493-6.

241. Vivanti AJ, Vauloup-Fellous C, Prevot S, et al. Transplacental transmission of SARS-CoV-2 infection. *Nat Commun* 2020; 11: 3572. 2020/07/16. DOI: 10.1038/s41467-020-17436-6.

242. Facchetti F, Bugatti M, Drera E, et al. SARS-CoV2 vertical transmission with adverse effects on the newborn revealed through integrated immunohistochemical, electron microscopy and molecular analyses of Placenta. *EBioMedicine* 2020; 59: 102951. 2020/08/21. DOI: 10.1016/j.ebiom.2020.102951.

243. Fenizia C, Biasin M, Cetin I, et al. Analysis of SARS-CoV-2 vertical transmission during pregnancy. *Nat Commun* 2020; 11: 5128. 2020/10/14. DOI: 10.1038/s41467-020-18933-4.

244. Parsa Y, Shokri N, Jahedbozorgan T, et al. Possible Vertical Transmission of COVID-19 to the Newborn; a Case Report. *Arch Acad Emerg Med* 2021; 9: e5. 2020/12/15.

245. Zeng L, Xia S, Yuan W, et al. Neonatal Early-Onset Infection With SARS-CoV-2 in 33 Neonates Born to Mothers With COVID-19 in Wuhan, China. *JAMA Pediatr* 2020 2020/03/28. DOI: 10.1001/jamapediatrics.2020.0878.

246. Alzamora MC, Paredes T, Caceres D, et al. Severe COVID-19 during Pregnancy and Possible Vertical Transmission. *Am J Perinatol* 2020 2020/04/19. DOI: 10.1055/s-0040-1710050.

247. Khan S, Jun L, Nawsherwan, et al. Association of COVID-19 with pregnancy outcomes in health-care workers and general women. *Clin Microbiol Infect* 2020 2020/04/12. DOI: 10.1016/j.cmi.2020.03.034.

248. Knight M, Bunch K, Vousden N, et al. Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study. *BMJ* 2020; 369: m2107. 2020/06/10. DOI: 10.1136/bmj.m2107.

249. Sisman J, Jaleel MA, Moreno W, et al. Intrauterine Transmission of Sars-Cov-2 Infection in a Preterm Infant. *Pediatr Infect Dis J* 2020 2020/07/14. DOI: 10.1097/INF.0000000000002815.

250. Kirtsman M, Diambomba Y, Poutanen SM, et al. Probable congenital SARS-CoV-2 infection in a neonate born to a woman with active SARS-CoV-2 infection. *CMAJ* 2020; 192: E647-E650. 2020/05/16. DOI: 10.1503/cmaj.200821.

251. Schwartz DA, Mohagheghi P, Beigi B, et al. Spectrum of neonatal COVID-19 in Iran: 19 infants with SARS-CoV-2 perinatal infections with varying test results, clinical findings and outcomes. *J Matern Fetal Neonatal Med* 2020: 1-10. 2020/08/14. DOI: 10.1080/14767058.2020.1797672.

252. Alamar I, Abu-Arja MH, Heyman T, et al. A Possible Case of Vertical Transmission of SARS-CoV-2 in a Newborn with Positive Placental In Situ Hybridization of SARS-CoV-2 RNA. *J Pediatric Infect Dis Soc* 2020 2020/09/06. DOI: 10.1093/jpids/piaa109.

253. Hinojosa-Velasco A, de Oca PVB, Garcia-Sosa LE, et al. A Case Report of Newborn Infant with Severe COVID-19 in Mexico: Detection of SARS-CoV-2 in Human Breast Milk and Stool. *Int J Infect Dis* 2020 2020/08/30. DOI: 10.1016/j.ijid.2020.08.055.

254. Marzollo R, Aversa S, Prefumo F, et al. Possible Coronavirus Disease 2019 Pandemic and Pregnancy: Vertical Transmission Is Not Excluded. *Pediatr Infect Dis J* 2020; 39: e261-e262. 2020/08/03. DOI: 10.1097/INF.0000000000002816.

255. Singh MV, Shrivastava A, Maurya M, et al. Vertical Transmission of SARS-CoV-2 from an Asymptomatic Pregnant Woman in India. *J Trop Pediatr* 2020 2020/09/26. DOI: 10.1093/tropej/fmaa048.

256. Diaz-Corvillon P, Monckeberg M, Barros A, et al. Routine screening for SARS CoV-2 in unselected pregnant women at delivery. *PLoS One* 2020; 15: e0239887. 2020/09/30. DOI: 10.1371/journal.pone.0239887.

257. Hascoët J, Jellimann J, Hartard C, et al. Case series of COVID-19 asymptomatic newborns with possible intrapartum transmission of SARS-CoV-2. *Frontiers in Pediatrics* 2020.

258. Alwardi TH, Ramdas V, Al Yahmadi M, et al. IS VERTICAL TRANSMISSION OF SARS-CoV-2 INFECTION POSSIBLE IN PRETERM TRIPLET PREGNANCY? A CASE SERIES. *Pediatr Infect Dis J* 2020 2020/10/03. DOI: 10.1097/INF.0000000000002926.

259. Gupta A, Malhotra Y, Patil U, et al. In Utero Vertical Transmission of Coronavirus Disease 2019 in a Severely Ill 29-week Preterm Infant. *AJP Rep* 2020; 10: e270-e274. 2020/10/24. DOI: 10.1055/s-0040-1715177.

260. Rivera-Hernandez P, Nair J, Islam S, et al. Coronavirus Disease 2019 in a Premature Infant: Vertical Transmission and Antibody Response or Lack Thereof. *AJP Rep* 2020; 10: e224-e227. 2020/10/24. DOI: 10.1055/s-0040-1715176.

261. Correia CR, Marcal M, Vieira F, et al. Congenital SARS-CoV-2 Infection in a Neonate With Severe Acute Respiratory Syndrome. *Pediatr Infect Dis J* 2020 2020/10/17. DOI: 10.1097/INF.0000000000002941.

262. Mohakud NK, Yerru H, Jr., Rajguru M, et al. An Assumed Vertical Transmission of SARS-CoV-2 During Pregnancy: A Case Report and Review of Literature. *Cureus* 2020; 12: e10659. 2020/11/03. DOI: 10.7759/cureus.10659.

263. Majachani N, Francois JLM, Fernando AK, et al. A Case of a Newborn Baby Girl Infected with SARS-CoV-2 Due to Transplacental Viral Transmission. *Am J Case Rep* 2020; 21: e925766. 2020/10/26. DOI: 10.12659/AJCR.925766.

264. Bandyopadhyay T, Sharma A, Kumari P, et al. Possible Early Vertical Transmission of COVID-19 from an Infected Pregnant Female to Her Neonate: A Case Report. *J Trop Pediatr* 2020 2020/11/23. DOI: 10.1093/tropej/fmaa094.

265. Hopwood AJ, Jordan-Villegas A, Gutierrez LD, et al. SARS-CoV-2 pneumonia in a newborn treated with remdesivir and COVID-19 convalescent plasma. *J Pediatric Infect Dis Soc* 2020 2020/12/12. DOI: 10.1093/jpids/piaa165.

266. Gaunt P, Ahmed I, Geethanath R, et al. Transmission of SARS-CoV-2 to premature twins from an asymptomatic mother. *Case Reports Perinatal Medicine* 2020; 9.

267. Pessoa FS, Vale MSD, Marques PF, et al. Probable vertical transmission identified within six hours of life. *Rev Assoc Med Bras (1992)* 2020; 66: 1621-1624. 2020/12/18. DOI: 10.1590/1806-9282.66.12.1621.

268. Bachani S, Arora R, Dabral A, et al. Clinical Profile, Viral Load, Maternal-Fetal Outcomes of Pregnancy With COVID-19: 4-Week Retrospective, Tertiary Care Single-Centre Descriptive Study. *J Obstet Gynaecol Can* 2020 2020/12/23. DOI: 10.1016/j.jogc.2020.09.021.

269. Carbayo-Jimenez T, Carrasco-Colom J, Epalza C, et al. Severe Acute Respiratory Syndrome Coronavirus 2 Vertical Transmission from an Asymptomatic Mother. *Pediatr Infect Dis J* 2021; 40: e115-e117. 2021/02/11. DOI: 10.1097/INF.0000000000003028.

270. Sharma R, Seth S, Sharma R, et al. Perinatal outcome and possible vertical transmission of coronavirus disease 2019: experience from North India. *Clin Exp Pediatr* 2021 2021/02/18. DOI: 10.3345/cep.2020.01704.

271. Birindwa EK, Mulumeoderhwa GM, Nyakio O, et al. A case study of the first pregnant woman with COVID-19 in Bukavu, eastern Democratic Republic of the Congo. *Matern Health Neonatol Perinatol* 2021; 7: 6. 2021/01/22. DOI: 10.1186/s40748-021-00127-5.

272. Singh VC, A.//Datta, M. R.//Ray, A. Maternal and Neonatal Outcomes of COVID-19 in Pregnancy: A Single-Centre Observational Study. *Cureus* 2021; 13: e13184.

273. Wang S, Guo L, Chen L, et al. A case report of neonatal COVID-19 infection in China. *Clin Infect Dis* 2020 2020/03/13. DOI: 10.1093/cid/ciaa225.

274. Nie R and al. e. Clinical features and the maternal and neonatal outcomes of pregnant women with coronavirus disease 2019. *medRxiv* 2020; NOT PEER REVIEWED.

275. Hu X, Gao J, Luo X, et al. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Vertical Transmission in Neonates Born to Mothers With Coronavirus Disease 2019 (COVID-19) Pneumonia. *Obstet Gynecol* 2020 2020/04/26. DOI: 10.1097/AOG.0000000000003926.

276. Lima ARO, Cardoso CC, Bentim PRB, et al. Maternal SARS-CoV-2 infection associated to systemic inflammatory response and pericardial effusion in the newborn: a Case-Report. *J Pediatric Infect Dis Soc* 2020 2020/10/31. DOI: 10.1093/jpids/piaa133.

277. Von Kohorn I, Stein SR, Shikani BT, et al. In Utero SARS-CoV-2 Infection. *J Pediatric Infect Dis Soc* 2020 2020/10/23. DOI: 10.1093/jpids/piaa127.

278. Hsu AL, Guan M, Johannesen E, et al. Placental SARS-CoV-2 in a Pregnant Woman with Mild COVID-19 Disease. *J Med Virol* 2020 2020/08/05. DOI: 10.1002/jmv.26386.

279. Debelenko L, Katsyv I, Chong AM, et al. Trophoblast damage with acute and chronic intervillositis: disruption of the placental barrier by severe acute respiratory syndrome coronavirus 2. *Hum Pathol* 2020; 109: 69-79. 2020/12/16. DOI: 10.1016/j.humpath.2020.12.004.

280. Cribiu FM, Erra R, Pugni L, et al. Severe SARS-CoV-2 placenta infection can impact neonatal outcome in the absence of vertical transmission. *Journal of Clinical Investigation* 2021; 131 (6) (no pagination).

281. Shende P, Gaikwad P, Gandhewar M, et al. Persistence of SARS-CoV-2 in the first trimester placenta leading to transplacental transmission and fetal demise from an asymptomatic mother. *Hum Reprod* 2020 2020/12/22. DOI: 10.1093/humrep/deaa367.

282. Valdespino-Vazquez MY, Helguera-Repetto CA, Leon-Juarez M, et al. Fetal and placental infection with SARS-CoV-2 in early pregnancy. *Journal of Medical Virology* 2021; 25: 25.

283. Stonoga ETS, de Almeida Lanzoni L, Rebutini PZ, et al. Intrauterine Transmission of SARS-CoV-2. *Emerg Infect Dis* 2021; 27: 638-641. 2020/11/14. DOI: 10.3201/eid2702.203824.

284. Agarwal M, Basumatary S, Kant B, et al. Intrauterine Transmission of SARS-CoV-2 (COVID-19 Virus). *Journal of Obstetrics & Gynaecology of India* 2021: 1-3.

285. Halici-Ozturk F, Ocal FD, Aydin S, et al. Investigating the risk of maternal-fetal transmission of SARS-CoV-2 in early pregnancy. *Placenta* 2021; 106: 25-29. 2021/02/22. DOI: 10.1016/j.placenta.2021.02.006.

286. Zeng H, Xu C, Fan J, et al. Antibodies in Infants Born to Mothers With COVID-19 Pneumonia. *JAMA* 2020 2020/03/28. DOI: 10.1001/jama.2020.4861.

287. Sileo FG, Tramontano AL, Leone C, et al. Pregnant woman infected by Coronavirus Disease (COVID-19) and calcifications of the fetal bowel and gallbladder: a case report. *Minerva Ginecol* 2020 2020/12/01. DOI: 10.23736/S0026-4784.20.04717-6.

288. Gao J, Li W, Hu X, et al. Disappearance of SARS-CoV-2 Antibodies in Infants Born to Women with COVID-19, Wuhan, China. *Emerg Infect Dis* 2020; 26 2020/07/06. DOI: 10.3201/eid2610.202328.

289. Dashraath P, Jing Lin Jeslyn W, Mei Xian Karen L, et al. Coronavirus Disease 2019 (COVID-19) Pandemic and Pregnancy. *Am J Obstet Gynecol* 2020 2020/03/29. DOI: 10.1016/j.ajog.2020.03.021.

290. Rubio Lorente AM, Pola Guillen M, Lopez Jimenez N, et al. Study of amniotic fluid in pregnant women infected with SARS-CoV-2 in first and second trimester. Is there evidence of vertical transmission? *The Journal of Maternal-Fetal & Neonatal Medicine* 2020.

291. Gao X, Wang S, Zeng W, et al. Clinical and immunologic features among COVID-19-affected mother-infant pairs: antibodies to SARS-CoV-2 detected in breast milk. *New Microbes New Infect* 2020; 37: 100752. 2020/09/10. DOI: 10.1016/j.nmni.2020.100752.

292. Chu H, Li J, Yan J, et al. Persistent SARS-CoV-2 RNA Positive in Feces but Negative in Breastmilk: A Case Report of COVID-19 in a Breastfeeding Patient. *Front Med (Lausanne)* 2020; 7: 562700. 2020/12/22. DOI: 10.3389/fmed.2020.562700.

293. Thanigainathan S, Kaliyaperumal V, Sivanandan S, et al. Is SARS-CoV-2 Transmitted Through Breastfeeding? *Indian J Pediatr* 2021 2021/02/09. DOI: 10.1007/s12098-021-03681-0.

294. Pace RM, Williams JE, Jarvinen KM, et al. Characterization of SARS-CoV-2 RNA, Antibodies, and Neutralizing Capacity in Milk Produced by Women with COVID-19. *mBio* 2021; 12 2021/02/11. DOI: 10.1128/mBio.03192-20.

295. Kumar J, Meena J, Yadav A, et al. SARS-CoV-2 detection in human milk: a systematic review. *J Matern Fetal Neonatal Med* 2021: 1-8. 2021/02/09. DOI: 10.1080/14767058.2021.1882984.

296. Wu Y, Liu C, Dong L, et al. Viral shedding of COVID-19 in pregnant women. *SSRN* 2020; PREPRINT.

297. Gross R, Conzelmann C, Muller JA, et al. Detection of SARS-CoV-2 in human breastmilk. *Lancet* 2020; 395: 1757-1758. 2020/05/25. DOI: 10.1016/S0140-6736(20)31181-8.

298. Bastug A, Hanifehnezhad A, Tayman C, et al. Virolactia in an Asymptomatic Mother with COVID-19. *Breastfeed Med* 2020 2020/07/03. DOI: 10.1089/bfm.2020.0161.

299. Krogstad P, Contreras D, Ng H, et al. No Evidence of Infectious SARS-CoV-2 in Human Milk: Analysis of a Cohort of 110 Lactating Women. *medRxiv 20210405212548897 PREPRINT* 2021. DOI: 10.1101/2021.04.05.21254897.

300. Chambers C, Krogstad P, Bertrand K, et al. Evaluation for SARS-CoV-2 in Breast Milk From 18 Infected Women. *JAMA* 2020; 324: 1347-1348. 2020/08/22. DOI: 10.1001/jama.2020.15580.

301. Pereira A, Cruz-Melguizo S, Adrien M, et al. Breastfeeding mothers with COVID-19 infection: a case series. *Int Breastfeed J* 2020; 15: 69. 2020/08/11. DOI: 10.1186/s13006-020-00314-8.

302. Lugli L, Bedetti L, Lucaccioni L, et al. An Uninfected Preterm Newborn Inadvertently Fed SARS-CoV-2-Positive Breast Milk. *Pediatrics* 2020; 146 2020/08/28. DOI: 10.1542/peds.2020-004960.

303. Kilic T, Kilic S, Kirici Berber N, et al. Investigation of SARS-CoV-2 RNA in Milk Produced by Women with COVID-19 and Follow-Up of Their Infants: A Preliminary Study. *International Journal of Clinical Practice* 2021: e14175.

304. World Health Organization. *Breastfeeding and COVID-19.* 23 June 2020 2020. Geneva: World Health Organization.

305. Ferrazzi E, Frigerio L, Savasi V, et al. Vaginal delivery in SARS-CoV-2 infected pregnant women in Northern Italy: a retrospective analysis. *BJOG* 2020 2020/04/28. DOI: 10.1111/1471-0528.16278.

306. Qiu H, Wu J, Hong L, et al. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study. *Lancet Infect Dis* 2020 2020/03/30. DOI: 10.1016/S1473-3099(20)30198-5.

307. Danis K, Epaulard O, Benet T, et al. Cluster of coronavirus disease 2019 (Covid-19) in the French Alps, 2020. *Clin Infect Dis* 2020 2020/04/12. DOI: 10.1093/cid/ciaa424.

308. Kan MJ, Grant LMC, Muna MA, et al. Fever without a source in a young infant due to SARS-CoV-2. *J Pediatric Infect Dis Soc* 2020 2020/04/23. DOI: 10.1093/jpids/piaa044.

309. Namasivayam A, Soe T and Palman J. Atypical case of COVID-19 in a critically unwell 5-week old infant. *BMJ Case Rep* 2020; 13 2020/09/16. DOI: 10.1136/bcr-2020-237142.

310. Mao ZQ, Wan R, He LY, et al. The enlightenment from two cases of asymptomatic infection with SARS-CoV-2: is it safe after 14 days of isolation? *Int J Infect Dis* 2020 2020/04/07. DOI: 10.1016/j.ijid.2020.03.041.

311. Scalinci SZ and Trovato Battagliola E. Conjunctivitis can be the only presenting sign and symptom of COVID-19. *IDCases* 2020; 20: e00774. 2020/05/07. DOI: 10.1016/j.idcr.2020.e00774.

312. Verdoni L, Mazza A, Gervasoni A, et al. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. *Lancet* 2020; 395: 1771-1778. 2020/05/16. DOI: 10.1016/S0140-6736(20)31103-X.

313. Whittaker E, Bamford A, Kenny J, et al. Clinical Characteristics of 58 Children With a Pediatric Inflammatory Multisystem Syndrome Temporally Associated With SARS-CoV-2. *JAMA* 2020 2020/06/09. DOI: 10.1001/jama.2020.10369.

314. Sadiq M, Aziz OA, Kazmi U, et al. Multisystem inflammatory syndrome associated with COVID-19 in children in Pakistan. *Lancet Child Adolesc Health* 2020 2020/08/14. DOI: 10.1016/S2352-4642(20)30256-X.

315. Bataille V, Visconti A, Rossi N, et al. Diagnostic value of skin manifestations of SARS-CoV-2 infection. *medRxiv* 2020; PREPRINT. DOI: **https://doi.org/10.1101/2020.07.10.20150656**.

316. Hormati A. SA, Afifian M., Khodadust F., Ahmadpour S. Can COVID-19 present unusual GI symptoms? *Journal of Microbiology, Immunology and Infection* 2020; In press, Journal Pre-proof.

317. Tay HS and Harwood R. Atypical presentation of COVID-19 in a frail older person. *Age Ageing* 2020 2020/04/22. DOI: 10.1093/ageing/afaa068.

318. Spiteri G, Fielding J, Diercke M, et al. First cases of coronavirus disease 2019 (COVID-19) in the WHO European Region, 24 January to 21 February 2020. *Euro Surveill* 2020; 25 2020/03/12. DOI: 10.2807/1560-7917.ES.2020.25.9.2000178.

319. Jiang X, Luo M, Zou Z, et al. Asymptomatic SARS-CoV-2 infected case with viral detection positive in stool but negative in nasopharyngeal samples lasts for 42 days. *J Med Virol* 2020 2020/04/25. DOI: 10.1002/jmv.25941.

320. Wan R, Mao ZQ, He LY, et al. Evidence from two cases of asymptomatic infection with SARS-CoV-2: Are 14 days of isolation sufficient? *Int J Infect Dis* 2020; 95: 174-175. 2020/04/07. DOI: 10.1016/j.ijid.2020.03.041.

321. Liu Z, Chu R, Gong L, et al. The assessment of transmission efficiency and latent infection period on asymptomatic carriers of SARS-CoV-2 infection. *Int J Infect Dis* 2020 2020/06/17. DOI: 10.1016/j.ijid.2020.06.036.

322. Hu S, Wang W, Wang Y, et al. Infectivity, susceptibility, and risk factors associated with SARS-CoV-2 transmission under intensive contact tracing in Hunan, China. . *medRxiv* 2020; PRE-PRINT.

323. Bae SH, Shin H, Koo HY, et al. Asymptomatic Transmission of SARS-CoV-2 on Evacuation Flight. *Emerg Infect Dis* 2020; 26 2020/08/22. DOI: 10.3201/eid2611.203353.

324. Kasper MR, Geibe JR, Sears CL, et al. An Outbreak of Covid-19 on an Aircraft Carrier. *N Engl J Med* 2020 2020/11/12. DOI: 10.1056/NEJMoa2019375.

325. Rajme-Lopez S, Gonzalez-Lara MF, Ortiz-Brizuela E, et al. Large scale screening for SARS-CoV-2 among healthcare workers: prevalence and risk factors for asymptomatic/pauci-symptomatic carriers, with emphasis on PPE use. *Infect Control Hosp Epidemiol* 2021: 1-17. 2021/02/25. DOI: 10.1017/ice.2021.68.

326. Ochiai D, Kasuga Y, Iida M, et al. Universal screening for SARS-CoV-2 in asymptomatic obstetric patients in Tokyo, Japan. *Int J Gynaecol Obstet* 2020 2020/06/05. DOI: 10.1002/ijgo.13252.

327. Buitrago-Garcia D, Egli-Gany D, Counotte MJ, et al. Occurrence and transmission potential of asymptomatic and presymptomatic SARS-CoV-2 infections: A living systematic review and meta-analysis. *PLoS Med* 2020; 17: e1003346. 2020/09/23. DOI: 10.1371/journal.pmed.1003346.

328. Bai Y, Yao L, Wei T, et al. Presumed Asymptomatic Carrier Transmission of COVID-19. *Jama* 2020; 21.

329. Rothe C, Schunk M, Sothmann P, et al. Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany. *The New England journal of medicine* 2020; 30. Letter.

330. Hu Z, Song C, Xu C, et al. Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China. *Sci China Life Sci* 2020; 63: 706-711. 2020/03/09. DOI: 10.1007/s11427-020-1661-4.

331. Zhou R, Li F, Chen F, et al. Viral dynamics in asymptomatic patients with COVID-19. *Int J Infect Dis* 2020; 96: 288-290. 2020/05/22. DOI: 10.1016/j.ijid.2020.05.030.

332. Han T, Hua L, He S, et al. The epidemiological characteristics of cluster transmission of coronavirus disease 2019 (COVID-19): a multi-center study in Jiangsu Province. *Am J Transl Res* 2020; 12: 6434-6444. 2020/11/17.

333. Huang N, Perez P, Kato T, et al. SARS-CoV-2 infection of the oral cavity and saliva. *Nature medicine* 2021; 25.

334. Qiu X, Nergiz AI, Maraolo AE, et al. Defining the role of asymptomatic and pre-symptomatic SARS-CoV-2 transmission - a living systematic review. *Clin Microbiol Infect* 2021 2021/01/24. DOI: 10.1016/j.cmi.2021.01.011.

335. Kong W, Wang Y, Hu J, et al. Comparison of clinical and epidemiological characteristics of asymptomatic and symptomatic SARS-CoV-2 infection: A multi-center study in Sichuan Province, China. *Travel Med Infect Dis* 2020: 101754. 2020/06/04. DOI: 10.1016/j.tmaid.2020.101754.

336. Xiao T and al. e. Early viral clearance and antibody kinetics of COVID-19 among asymptomatic carrieres. . *MedRxiv* 2020; NOT PEER REVIEWED.

337. Lin J, Duan J, Tan T, et al. The isolation period should be longer: Lesson from a child infected with SARS-CoV-2 in Chongqing, China. *Pediatr Pulmonol* 2020; 55: E6-E9. 2020/04/04. DOI: 10.1002/ppul.24763.

338. Diercks GR, Park BJ, Myers LB, et al. Asymptomatic COVID-19 infection in a child with nasal foreign body. *Int J Pediatr Otorhinolaryngol* 2020; 135: 110092. 2020/06/02. DOI: 10.1016/j.ijporl.2020.110092.

339. Han MS, Choi EH, Chang SH, et al. Clinical Characteristics and Viral RNA Detection in Children With Coronavirus Disease 2019 in the Republic of Korea. *JAMA Pediatr* 2020 2020/08/29. DOI: 10.1001/jamapediatrics.2020.3988.

340. Stock AD, Bader ER, Cezayirli P, et al. COVID-19 infection among healthcare workers: serological findings supporitng routine testing. *Fontiers in Medicine* 2020; 7.

341. Shields A, Faustini SE, Perez-Toledo M, et al. SARS-CoV-2 seroprevalence and asymptomatic viral carriage in healthcare workers: a cross-sectional study. *Thorax* 2020 2020/09/13. DOI: 10.1136/thoraxjnl-2020-215414.

342. Treibel TA, Manisty C, Burton M, et al. COVID-19: PCR screening of asymptomatic health-care workers at London hospital. *The Lancet* 2020. DOI: **https://doi.org/10.1016/S0140-6736(20)31100-4**.

343. Patel MC, Chaisson LH, Borgetti S, et al. Asymptomatic SARS-CoV-2 infection and COVID-19 mortality during an outbreak investigation in a skilled nursing facility. *Clin Infect Dis* 2020 2020/06/18. DOI: 10.1093/cid/ciaa763.

344. Corcorran MA, Olin S, Rani G, et al. Prolonged persistence of PCR-detectable virus during an outbreak of SARS-CoV-2 in an inpatient geriatric psychiatry unit in King County, Washington. *Am J Infect Control* 2020 2020/08/23. DOI: 10.1016/j.ajic.2020.08.025.

345. Hijnen D, Marzano AV, Eyerich K, et al. SARS-CoV-2 Transmission from Presymptomatic Meeting Attendee, Germany. *Emerg Infect Dis* 2020; 26 2020/05/12. DOI: 10.3201/eid2608.201235.

346. Wei W.E. LZ, Chiew C.J., Yong S.E., Toh M.T., Lee V.J. Presymptomatic transmission of SARS-CoV-2 - Singapore, January 23-Marxh 16, 2020. *Morbidity and Mortality Weekly Report* 2020; 69 - Early Release.

347. Tong ZD, Tang A, Li KF, et al. Potential Presymptomatic Transmission of SARS-CoV-2, Zhejiang Province, China, 2020. *Emerging infectious diseases* 2020; 26.

348. Huang L, Zhang X, Zhang X, et al. Rapid asymptomatic transmission of COVID-19 during the incubation period demonstrating strong infectivity in a cluster of youngsters aged 16-23 years outside Wuhan and characteristics of young patients with COVID-19: A prospective contact-tracing study. *J Infect* 2020 2020/04/14. DOI: 10.1016/j.jinf.2020.03.006.

349. Gao Y, Shi C, Chen Y, et al. A cluster of the Corona Virus Disease 2019 caused by incubation period transmission in Wuxi, China. *J Infect* 2020 2020/04/14. DOI: 10.1016/j.jinf.2020.03.042.

350. Bohmer MM, Buchholz U, Corman VM, et al. Investigation of a COVID-19 outbreak in Germany resulting from a single travel-associated primary case: a case series. *Lancet Infect Dis* 2020 2020/05/19. DOI: 10.1016/S1473-3099(20)30314-5.

351. Chen M, Fan P, Liu Z, et al. A SARS-CoV-2 familial cluster infection reveals asymptomatic transmission to children. *J Infect Public Health* 2020; 13: 883-886. 2020/06/09. DOI: 10.1016/j.jiph.2020.05.018.

352. Sang H, Cui Y, Lai X, et al. A familial cluster of coronavirus disease 2019 (COVID-19) caused by one family member during his asymptomatic incubation period. *J Public Health (Oxf)* 2020 2020/07/11. DOI: 10.1093/pubmed/fdaa098.

353. Chun JY, Baek G and Kim Y. Transmission onset distribution of COVID-19. *Int J Infect Dis* 2020 2020/08/11. DOI: 10.1016/j.ijid.2020.07.075.

354. Ren X, Li Y, Yang X, et al. Evidence for pre-symptomatic transmission of coronavirus disease 2019 (COVID-19) in China. *Influenza Other Respir Viruses* 2020 2020/08/09. DOI: 10.1111/irv.12787.

355. Gong X, Xiao W, Cui Y, et al. Three infection clusters related with potential pre-symptomatic transmission of coronavirus disease (COVID-19), Shanghai, China, January to February 2020. *Euro Surveill* 2020; 25 2020/08/22. DOI: 10.2807/1560-7917.ES.2020.25.33.2000228.

356. Zhang Y, Muscatello D, Tian Y, et al. Role of presymptomatic transmission of COVID-19: evidence from Beijing, China. *J Epidemiol Community Health* 2020 2020/08/29. DOI: 10.1136/jech-2020-214635.

357. Lai X, Wang M, Qin C, et al. Coronavirus Disease 2019 (COVID-2019) Infection Among Health Care Workers and Implications for Prevention Measures in a Tertiary Hospital in Wuhan, China. *JAMA Netw Open* 2020; 3: e209666. 2020/05/22. DOI: 10.1001/jamanetworkopen.2020.9666.

358. Kluytmans-van den Bergh M.F.Q. BAGM, Pas S.D., Bentvelsen R.G., van den Bijllaardt W., van Oudheusden A.J.G., van Rijen M.M.L., Verweij J.J., Koopmans M.P.G., Kluytmans J.A.J.W. . SARS-CoV-2 infection in 86 healthcare workers in two Dutch hospitals in March 2020. *medRxiv* 2020; NOT PEER REVIEWED.

359. Wang X, Zhou Q, He Y, et al. Nosocomial outbreak of COVID-19 pneumonia in Wuhan, China. *Eur Respir J* 2020; 55 2020/05/06. DOI: 10.1183/13993003.00544-2020.

360. Jewkes SV, Zhang Y and Nicholl DJ. Nosocomial spread of COVID-19: lessons learned from an audit on a stroke/neurology ward in a UK district general hospital. *Clin Med (Lond)* 2020; 20: e173-e177. 2020/07/29. DOI: 10.7861/clinmed.2020-0422.

361. Davis P, Gibson R, Wright E, et al. Atypical presentations in the hospitalised older adult testing positive for SARS-CoV-2: a retrospective observational study in Glasgow,

Scotland. *Scott Med J* 2020: 36933020962891. 2020/10/13. DOI: 10.1177/0036933020962891.

362. Rickman HM, Rampling T, Shaw K, et al. Nosocomial transmission of COVID-19: a retrospective study of 66 hospital-acquired cases in a London teaching hospital. *Clin Infect Dis* 2020 2020/06/21. DOI: 10.1093/cid/ciaa816.

363. Khonyongwa K, Taori SK, Soares A, et al. Incidence and outcomes of healthcare-associated COVID-19 infections: significance of delayed diagnosis and correlation with staff absence. *J Hosp Infect* 2020 2020/10/17. DOI: 10.1016/j.jhin.2020.10.006.

364. Asad H, Johnston C, Blyth I, et al. Health care workers and patients as Trojan horses: a COVID19 ward outbreak. *Infection Prevention in Practice* 2020; 2.

365. Schwierzeck V, Konig JC, Kuhn J, et al. First reported nosocomial outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in a pediatric dialysis unit. *Clin Infect Dis* 2020 2020/04/28. DOI: 10.1093/cid/ciaa491.

366. Wei XS, Wang XR, Zhang JC, et al. A cluster of health care workers with COVID-19 pneumonia caused by SARS-CoV-2. *J Microbiol Immunol Infect* 2020 2020/05/04. DOI: 10.1016/j.jmii.2020.04.013.

367. Dantes RB, Jones TT and Neujahr DC. Delayed Recognition of Community Transmission of COVID-19 Resulting in Healthcare Worker Infections. *Infect Control Hosp Epidemiol* 2020: 1-6. 2020/06/11. DOI: 10.1017/ice.2020.285.

368. Shah ASV, Wood R, Gribben C, et al. Risk of hospital admission with coronavirus disease 2019 in healthcare workers and their households: nationwide linkage cohort study. *BMJ* 2020; 371: m3582. 2020/10/30. DOI: 10.1136/bmj.m3582.

369. Hunter E, Price DA, Murphy E, et al. First experience of COVID-19 screening of health-care workers in England. *Lancet* 2020; 395: e77-e78. 2020/04/26. DOI: 10.1016/S0140-6736(20)30970-3.

370. Folgueira MD and al. e. SARS-CoV-2 infection in health care workers in a large public hospital in Madrid, Spain, during March 2020. . *MedRxiv* 2020; NOT PEER REVIEWED.

371. Sikkema RSea. COVID-19 in healthcare workers in three hospitals in the South of the Netherlands, March 2020. *medRxiv* 2020; UNPUBLISHED. DOI: **https://doi.org/10.1101/2020.04.26.20079418**.

372. Safdar N, Moreno GK, Braun KM, et al. Determining the source of transmission of SARS-CoV-2 infection in a healthcare worker. *medRxiv* 2020; PRE-PRINT. DOI: **https://doi.org/10.1101/2020.04.27.20077016**.

373. Lucey M, Macori G, Mullane N, et al. Whole-genome sequencing to track SARS-CoV-2 transmission in nosocomial outbreaks. *Clin Infect Dis* 2020 2020/09/22. DOI: 10.1093/cid/ciaa1433.

374. Parkulo MA, Brinker TM, Bosch W, et al. Risk of SARS-CoV-2 Transmission Among Coworkers in a Surgical Environment. *Mayo Clin Proc* 2021; 96: 152-155. 2021/01/09. DOI: 10.1016/j.mayocp.2020.10.016.

375. Francis RV, Billam H, Clarke M, et al. The impact of real-time whole genome sequencing in controlling healthcare associated SARS-CoV-2 outbreaks. *MedRxiv* 2021; PRE-PRINT.

376. Queromes G, Destras G, Bal A, et al. Characterization of SARS-CoV-2 ORF6 deletion variants detected in a nosocomial cluster during routine genomic surveillance, Lyon, France. *Emerg Microbes Infect* 2021: 1-56. 2021/01/06. DOI: 10.1080/22221751.2021.1872351.

377. Scientific Advisory Group for Emergencies. *Eighty-third SAGE meeting on COVID-19, 11 March 2021*. 11 March 2021 2021.

378. Rivett L, Sridhar S, Sparkes D, et al. Screening of healthcare workers for SARS-CoV-2 highlights the role of asymptomatic carriage in COVID-19 transmission. *Elife* 2020; 9 2020/05/12. DOI: 10.7554/eLife.58728.

379. Zabarsky TF, Bhullar D, Silva SY, et al. What are the sources of exposure in healthcare personnel with coronavirus disease 2019 infection? *Am J Infect Control* 2020 2020/08/17. DOI: 10.1016/j.ajic.2020.08.004.

380. Ladhani SN, Chow JY, Janarthanan R, et al. Investigation of SARS-CoV-2 outbreaks in six care homes in London, April 2020. *EClinicalMedicine* 2020: 100533. 2020/09/15. DOI: 10.1016/j.eclinm.2020.100533.

381. Kennelly SP, Dyer AH, Martin R, et al. Asymptomatic carriage rates and case-fatality of SARS-CoV-2 infection in residents and staff in Irish nursing homes. . *medRxiv* 2020; PRE-PRINT.

382. Healthcare Safety Investigation Branch. *COVID-19 transmission in hospitals: management of the risk - a prospective safety investigation. Independent report by the Healthcare Safety Investigation Branch I2020/018*. October 2020 2020.

383. Brandt MP, Jager W, Epple S, et al. SARS-CoV-2 outbreak in medical employees in a large urologic department: Spread, containment and outcome. *Am J Infect Control* 2021 2021/02/23. DOI: 10.1016/j.ajic.2021.02.011.

384. Sharma S, Mohindra R, Rana K, et al. Assessment of Potential Risk Factors for 2019-Novel Coronavirus (2019-nCov) Infection among Health Care Workers in a Tertiary Care Hospital, North India. *J Prim Care Community Health* 2021; 12: 21501327211002099. 2021/03/16. DOI: 10.1177/21501327211002099.

385. Davido B, Gautier S, Riom I, et al. The first wave of COVID-19 in hospital staff members of a tertiary care hospital in the greater Paris area: A surveillance and risk factors study. *Int J Infect Dis* 2021; 105: 172-179. 2021/02/20. DOI: 10.1016/j.ijid.2021.02.055.

386. Richterman A, Meyerowitz EA and Cevik M. Hospital-Acquired SARS-CoV-2 Infection: Lessons for Public Health. *JAMA* 2020 2020/11/14. DOI: 10.1001/jama.2020.21399.

387. Brown KA, Jones A, Daneman N, et al. Association Between Nursing Home Crowding and COVID-19 Infection and Mortality in Ontario, Canada. *JAMA Intern Med* 2021; 181: 229-236. 2020/11/10. DOI: 10.1001/jamainternmed.2020.6466.

388. Scottish Government. *Visiting guidance for hospitals in Scotland - Safely supporting visiting across Scotland's hospitals*. 2 December 2020 2020.

389. ARHAI Scotland. *Scottish COVID-19 infection prevention and control addendum for acute settings*. 27 October 2020 2020. National Infection Prevention and Control Manual: NHS National Services Scotland.

390. Canova V, Lederer Schlapfer H, Piso RJ, et al. Transmission risk of SARS-CoV-2 to healthcare workers -observational results of a primary care hospital contact tracing. *Swiss Med Wkly* 2020; 150: w20257. 2020/04/26. DOI: 10.4414/smw.2020.20257.

391. Wendt R, Nagel S, Nickel O, et al. Comprehensive investigation of an in-hospital transmission cluster of a symptomatic SARS-CoV-2-positive physician among patients and healthcare workers in Germany. *Infect Control Hosp Epidemiol* 2020: 1-3. 2020/06/04. DOI: 10.1017/ice.2020.268.

392. Ng K, Poon BH, Kiat Puar TH, et al. COVID-19 and the Risk to Health Care Workers: A Case Report. *Ann Intern Med* 2020; 172: 766-767. 2020/03/17. DOI: 10.7326/L20-0175.

393. Chow A, Htun HL, Kyaw WM, et al. Atypical COVID-19: Preventing transmission from unexpected cases. *Infect Control Hosp Epidemiol* 2020: 1-3. 2020/08/14. DOI: 10.1017/ice.2020.419.

394. Tillett RL, Sevinsky JR, Hartley PD, et al. Genomic evidence for reinfection with SARS-CoV-2: a case study. *Lancet Infect Dis* 2021; 21: 52-58. 2020/10/16. DOI: 10.1016/S1473-3099(20)30764-7.

395. Selhorst P, Van Ierssel S, Michiels J, et al. Symptomatic SARS-CoV-2 reinfection of a health care worker in a Belgian nosocomial outbreak despite primary neutralizing antibody response. *Clin Infect Dis* 2020 2020/12/15. DOI: 10.1093/cid/ciaa1850.

396. Van Elslande J, Vermeersch P, Vandervoort K, et al. Symptomatic SARS-CoV-2 reinfection by a phylogenetically distinct strain. *Clin Infect Dis* 2020 2020/09/06. DOI: 10.1093/cid/ciaa1330.

397. Prado-Vivar B, Becerrra-Wong M, Guadalupe JJ, et al. COVID-19 re-infection by a phylogenetically distince SARS-CoV-2 variant, first confirmed event in South America. *SSRN* 2020.

398. To KK, Hung IF, Ip JD, et al. COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing. *Clin Infect Dis* 2020 2020/08/26. DOI: 10.1093/cid/ciaa1275.

399. Gupta V, Bhoyar RC, Jain A, et al. Asymptomatic reinfection in two healthcare workers from India with genetically distinct SARS-CoV-2. *Clin Infect Dis* 2020 2020/09/24. DOI: 10.1093/cid/ciaa1451.

400. Harrington D, Kele B, Pereira S, et al. Confirmed Reinfection with SARS-CoV-2 Variant VOC-202012/01. *Clin Infect Dis* 2021 2021/01/10. DOI: 10.1093/cid/ciab014.

401. Fintelman-Rodrigues N, Da Silva A, d P, D., Cristina dos Santos M, et al. Viral genetic evidence and host immune response of a small cluster of case reports with two episodes of SARS-CoV-2 infection. *SSRN* 2021; PREPRINT.

402. Salehi-Vaziri MJ, T.//Farahmand, B.//Fotouhi, F.//Banifazl, M.//Pouriayevali, M. H.//Sadat Larijani, M.//Afzali, N.//Ramezani, A. Clinical characteristics of SARS-CoV-2 by re-infection vs. reactivation: a case series from Iran. *European Journal of Clinical Microbiology & Infectious Diseases* 2021; 18: 18.

403. Theo Brehm T, Pfefferle S, von Possel R, et al. SARS-CoV-2 Reinfection in a HealthcareWorker Despite the Presence of Detectable Neutralizing Antibodies. *Viruses* 2021; 13: 661.

404. Hall V, Foulkes S, Charlett A, et al. SARS-CoV-2 infection rates of antibody-positive compared with antibody-negative health-care workers in England: a large, multicentre, prospective cohort study (SIREN). *Lancet* 2021; 397: 1459-1469.

405. European Centre for Disease Prevention and Control. *Reinfection with SARS-CoV-2: considerations for public health response.* . 21 September 2020 2020.

406. European Centre for Disease Prevention and Control ECDC. Reinfection with SARS-CoV-2: implementation of a surveillance case definition within the EU/EEA. Technical report 8 April 2021, **https://www.ecdc.europa.eu/sites/default/files/documents/Reinfection-with-SARSCoV2-implementation-of-a-surveillance-case-definition.pdf** (2021, accessed 12 April 2021).

407. Pan American Health Organization and World Health Organization. *Interim guidelines for detecting cases of reinfection by SARS-CoV-2*. 29 October 2020 2020. Washington, D.C.

408. Public Health Scotland. *COVID-19: Information and guidance for social, community and residential care settings (excluding adult and older people care home settings) Version 1.6*. 24 December 2020 2020.

409. Scottish Government. *Coronavirus (COVID-19): asymptomatic staff testing in NHS Scotland*. 18 December 2020 2020.

410. Scottish Government. *Interim FAQ - Asymptomatic testing of patient-facing staff in NHS Scotland hospitals, the Scottish Ambulance Service, COVID-19 Assessment Centres, Community and District Nurses and COVID-19 vaccinators using lateral flow testing. Version 1.2*. 11 January 2021 2021.

411. ECDC. Technical Report. Risk of SARS-CoV-2 transmission from newly-infected individuals with documented previous infection or vaccination. 2021.

412. Boldog P, Tekeli T, Vizi Z, et al. Risk assessment of novel coronavirus COVID-19 outbreaks outside China. *Journal of Clinical Medicine* 2020; 9 (2) (no pagination).

413. Li Q, Guan X, Wu P, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. *The New England journal of medicine* 2020; 29.

414. Lauer SA, Grantz KH, Bi Q, et al. The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application. *Ann Intern Med* 2020 2020/03/10. DOI: 10.7326/M20-0504.

415. World Health Organization. *Report of the WHO-China Joint Commission on Coronavirus disease 2019.* 2020. World Health Organization.

416. Sohrabi C, Alsafi Z, O'Neill N, et al. World Health Organization declares Global Emergency: A review of the 2019 Novel Coronavirus (COVID-19). *International Journal Of Surgery* 2020; 26: 26. Review.

417. Tian S, Hu N, Lou J, et al. Characteristics of COVID-19 infection in Beijing. *Journal of Infection* 2020; 26: 26.

418. Backer JA, Klinkenberg D and Wallinga J. Incubation period of 2019 novel coronavirus (2019-nCoV) infections among travellers from Wuhan, China, 20-28 January 2020. *Euro Surveill* 2020; 25 2020/02/13. DOI: 10.2807/1560-7917.ES.2020.25.5.2000062.

419. Fan J, Liu X, Pan W, et al. Epidemiology of 2019 Novel Coronavirus Disease-19 in Gansu Province, China, 2020. *Emerg Infect Dis* 2020; 26 2020/03/14. DOI: 10.3201/eid2606.200251.

420. Jiang X, Rayner S and Luo MH. Does SARS-CoV-2 has a longer incubation period than SARS and MERS? *J Med Virol* 2020; 92: 476-478. 2020/02/15. DOI: 10.1002/jmv.25708.

421. COVID-19 National Emergency Response Center EaCMT, Korea Centers for Disease Control and Prevention,. Early epidemiological and clinical characteristics of 28 cases of coronavirus disease in South Korea. *Osong Public Health Research Perspective* 2020; 11: 8-14.

422. Zhang J, Litvinova M, Wang W, et al. Evolving epidemiology and transmission dynamics of coronavirus disease 2019 outside Hubei province, China: a descriptive and modelling study. *Lancet Infect Dis* 2020 2020/04/06. DOI: 10.1016/S1473-3099(20)30230-9.

423. Tindale LC, Stockdale JE, Coombe M, et al. Evidence for transmission of COVID-19 prior to symptom onset. *Elife* 2020; 9 2020/06/23. DOI: 10.7554/eLife.57149.

424. Zhao C, Xu Y, Zhang X, et al. Public health initiatives from hospitalized patients with COVID-19, China. *J Infect Public Health* 2020 2020/06/28. DOI: 10.1016/j.jiph.2020.06.013.

425. Yang L, Dai J, Zhao J, et al. Estimation of incubation period and serial interval of COVID-19: analysis of 178 cases and 131 transmission chains in Hubei province, China. *Epidemiol Infect* 2020; 148: e117. 2020/07/01. DOI: 10.1017/S0950268820001338.

426. Viego V, Geri M, Castiglia J, et al. Incubation period and serial interval of Covid-19 in a chain of infections in Bahia Blanca (Argentina). *Cien Saude Colet* 2020; 25: 3503-3510. 2020/09/03. DOI: 10.1590/1413-81232020259.20852020.

427. Lopez Bernal J, Panagiotopoulos N, Byers C, et al. Transmission dynamics of COVID-19 in household and community settings in the United Kingdom. *medRxiv* 2020; PREPRINT.

428. Health Information and Quality Authority. *Evidence summary for the incubation period of COVID-19, or time to first positive test, in individuals exposed to SARS-CoV-2.* 4 November 2020 2020.

429. Tan WYT, Wong LY, Leo YS, et al. Does incubation period of COVID-19 vary with age? A study of epidemiologically linked cases in Singapore. *Epidemiology and infection* 2020; 148: e197-e197. DOI: 10.1017/S0950268820001995.

430. Alene M, Yismaw L, Assemie MA, et al. Serial interval and incubation period of COVID-19: a systematic review and meta-analysis. *BMC Infectious Diseases* 2021; 21: 257. DOI: 10.1186/s12879-021-05950-x.

431. Elias C, Sekri A, Leblanc P, et al. The incubation period of COVID-19: A meta-analysis. *Int J Infect Dis* 2021; 104: 708-710. 2021/02/07. DOI: 10.1016/j.ijid.2021.01.069.

432. Deng SQ and Peng HJ. Characteristics of and public health responses to the coronavirus disease 2019 outbreak in China. *Journal of Clinical Medicine* 2020; 9 (2) (no pagination). Review.

433. Lillie PJ, Samson A, Li A, et al. Novel coronavirus disease (Covid-19): the first two patients in the UK with person to person transmission. *Journal of Infection* 2020; 28: 28. Letter.

434. Pung R, Chiew CJ, Young BE, et al. Investigation of three clusters of COVID-19 in Singapore: implications for surveillance and response measures. *Lancet* 2020; 395: 1039-1046. 2020/03/21. DOI: 10.1016/S0140-6736(20)30528-6.

435. Patrikar SR, Kotwal A, Bhatti VK, et al. Incubation Period and Reproduction Number for Novel Coronavirus 2019 (COVID-19) Infections in India. *Asia Pac J Public Health* 2020: 1010539520956427. 2020/09/01. DOI: 10.1177/1010539520956427.

436. Bender JK, Brandl M, Hohle M, et al. Analysis of Asymptomatic and Presymptomatic Transmission in SARS-CoV-2 Outbreak, Germany, 2020. *Emerg Infect Dis* 2021; 27 2021/02/19. DOI: 10.3201/eid2704.204576.

437. Xiao Z, Xie X, Guo W, et al. Examining the incubation period distributions of COVID-19 on Chinese patients with different travel histories. *J Infect Dev Ctries* 2020; 14: 323-327. 2020/05/08. DOI: 10.3855/jidc.12718.

438. Bi Q, Wu Y, Mei S, et al. Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study. *Lancet Infect Dis* 2020; 20: 911-919. 2020/05/01. DOI: 10.1016/S1473-3099(20)30287-5.

439. UK Government. UK Chief Medical Officers' statement on the self-isolation period: 11 December 2020. Department of Health & Social Care2020.

440. Marks M, Millat-Martinez P, Ouchi D, et al. Transmission of COVID-19 in 282 clusters in Catalonia, Spain: a cohort study. *Lancet Infect Dis* 2021 2021/02/06. DOI: 10.1016/S1473-3099(20)30985-3.

441. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020 2020/03/15. DOI: 10.1016/S0140-6736(20)30566-3.

442. Chen X, Hu W, Ling J, et al. Hypertension and diabetes delay the viral clearance in COVID-19 patients. *medRxiv* 2020; NOT PEER REVIEWED.

443. To KK, Tsang OT, Leung WS, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. *Lancet Infect Dis* 2020 2020/03/28. DOI: 10.1016/S1473-3099(20)30196-1.

444. He X, Lau EHY, Wu P, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nat Med* 2020 2020/04/17. DOI: 10.1038/s41591-020-0869-5.

445. Liu Y, Yan LM, Wan L, et al. Viral dynamics in mild and severe cases of COVID-19. *Lancet Infect Dis* 2020; 20: 656-657. 2020/03/23. DOI: 10.1016/S1473-3099(20)30232-2.

446. Chen PF, Yu XX, Liu YP, et al. Virus load and virus shedding of SARS-CoV-2 and their impact on patient outcomes. *World J Clin Cases* 2020; 8: 6252-6263. 2021/01/05. DOI: 10.12998/wjcc.v8.i24.6252.

447. Kim NJ, Choe PG, Park SJ, et al. A cluster of tertiary transmissions of 2019 novel coronavirus (SARS-CoV-2) in the community from infectors with common cold symptoms. *Korean J Intern Med* 2020 2020/06/09. DOI: 10.3904/kjim.2020.122.

448. Xiao AT, Tong YX, Gao C, et al. Dynamic profile of RT-PCR findings from 301 COVID-19 patients in Wuhan, China: A descriptive study. *J Clin Virol* 2020; 127: 104346. 2020/05/04. DOI: 10.1016/j.jcv.2020.104346.

449. Mallett S, Allen AJ, Graziadio S, et al. At what times during infection is SARS-CoV-2 detectable and no longer detectable using RT-PCR-based tests? A systematic review of individual participant data. *BMC Med* 2020; 18: 346. 2020/11/05. DOI: 10.1186/s12916-020-01810-8.

450. Kam KQ, Thoon KC, Maiwald M, et al. SARS-CoV-2 viral RNA load dynamics in the nasopharynx of infected children. *MedRxiv* 2020; PREPRINT.

451. Wang K, Zhang X, Sun J, et al. Differences of SARS-CoV-2 Shedding Duration in Sputum and Nasopharyngeal Swab Specimens among Adult Inpatients with COVID-19. *Chest* 2020 2020/06/23. DOI: 10.1016/j.chest.2020.06.015.

452. Saurabh S, Kumar R, Gupta MK, et al. Prolonged persistence of SARS-CoV-2 in the upper respiratory tract of asymptomatic infected individuals. *QJM* 2020 2020/07/02. DOI: 10.1093/qjmed/hcaa212.

453. AlJishi JM and Al-Tawfiq JA. Intermittent viral shedding in respiratory samples of patients with SARS-CoV-2: observational analysis with infection control implications. *J Hosp Infect* 2020 2020/09/14. DOI: 10.1016/j.jhin.2020.09.011.

454. Kim SM, Hwang YJ and Kwak Y. Prolonged SARS-CoV-2 detection and reversed RT-PCR results in mild or asymptomatic patients. *Infect Dis (Lond)* 2020: 1-7. 2020/09/17. DOI: 10.1080/23744235.2020.1820076.

455. Deng W, Guang TW, Yang M, et al. Positive results for patients with COVID-19 discharged form hospital in Chongqing, China. *BMC Infect Dis* 2020; 20: 429. 2020/06/21. DOI: 10.1186/s12879-020-05151-y.

456. Li W, Su YY, Zhi SS, et al. Viral shedding dynamics in asymptomatic and mildly symptomatic patients infected with SARS-CoV-2. *Clin Microbiol Infect* 2020 2020/07/13. DOI: 10.1016/j.cmi.2020.07.008.

457. Edwards T, Santos VS, Wilson AL, et al. Variation of SARS-CoV-2 viral loads by sample type, disease severity and time: a systematic review. . *MedRxiv* 2020; PRE-PRINT.

458. Kandetu TB, Dziuban EJ, Sikuvi K, et al. Persistence of positive RT-PCR results for over 70 days in two travelers with COVID-19. *Disaster Med Public Health Prep* 2020: 1-7. 2020/11/20. DOI: 10.1017/dmp.2020.450.

459. Fu Y, Li Y, Guo E, et al. Dynamics and Correlation Among Viral Positivity, Seroconversion, and Disease Severity in COVID-19 : A Retrospective Study. *Ann Intern Med* 2020 2020/12/08. DOI: 10.7326/M20-3337.

460. Ao Z, Li Y, Wei J, et al. Clinical characteristics and potential factors for recurrence of positive SARS-CoV-2 RNA in convalescent patients: a retrospective cohort study. *Clin Exp Med* 2021 2021/02/06. DOI: 10.1007/s10238-021-00687-y.

461. Garcia Abellan J, Padilla S, Fernandez Gonzalez M, et al. Long-term clinical, virological and immunological outcomes in patients hospitalized for COVID-19: antibody response predicts long COVID. (2021).

462. Tiwari L, Gupta P, Singh CM, et al. Persistent positivity of SARS-CoV-2 nucleic acid in asymptomatic healthcare worker: infective virion or inactive nucleic acid? *BMJ Case Rep* 2021; 14 2021/03/05. DOI: 10.1136/bcr-2020-241087.

463. Folgueira MD, Luczkowiak J, Lasala F, et al. Prolonged SARS-CoV-2 cell culture replication in respiratory samples from patients with severe COVID-19. *Clinical Microbiology and Infection*. DOI: 10.1016/j.cmi.2021.02.014.

464. Baang JH, Smith C, Mirabelli C, et al. Prolonged Severe Acute Respiratory Syndrome Coronavirus 2 Replication in an Immunocompromised Patient. *J Infect Dis* 2021; 223: 23-27. 2020/10/23. DOI: 10.1093/infdis/jiaa666.

465. Tarhini H, Recoing A, Bridier-Nahmias A, et al. Long term SARS-CoV-2 infectiousness among three immunocompromised patients: from prolonged viral shedding to SARS-CoV-2 superinfection. *J Infect Dis* 2021 2021/02/09. DOI: 10.1093/infdis/jiab075.

466. Alsaud AE, Nair AP, Matarneh AS, et al. Case Report: Prolonged Viral Shedding in Six COVID-19 Patients. *Am J Trop Med Hyg* 2021 2021/02/25. DOI: 10.4269/ajtmh.20-0933.

467. Rajakumar I, Isaac DL, Fine N, et al. Extensive Environmental Contamination and Prolonged Severe Acute Respiratory Coronavirus-2 Viability in Immunosuppressed Recent Heart Transplant Recipients with Clinical and Virologic Benefit with Remdesivir. *Infection Control & Hospital Epidemiology* 2021: 1-10.

468. Gombar S, Chang M, Hogan CA, et al. Persistent detection of SARS-CoV-2 RNA in patients and healthcare workers with COVID-19. *J Clin Virol* 2020; 129: 104477. 2020/06/09. DOI: 10.1016/j.jcv.2020.104477.

469. Mancuso P, Venturelli F, Vicentini M, et al. Temporal profile and determinants of viral shedding and of viral clearance confirmation on nasopharyngeal swabs from SARS-CoV-2-positive subjects: a population-based prospective cohort study in Reggio Emilia, Italy. *BMJ Open* 2020; 10: e040380. 2020/09/04. DOI: 10.1136/bmjopen-2020-040380.

470. Omar S, Bartz C, Becker S, et al. Duration of SARS-CoV-2 RNA detection in COVID-19 patients in home isolation, Rhineland-Palatinate, Germany, 2020 - an interval-censored survival analysis. *Euro Surveill* 2020; 25 2020/08/01. DOI: 10.2807/1560-7917.ES.2020.25.30.2001292.

471. Han C, Duan C, Zhang S, et al. Digestive Symptoms in COVID-19 Patients With Mild Disease Severity: Clinical Presentation, Stool Viral RNA Testing, and Outcomes. *The American journal of gastroenterology* 2020; 115: 916-923. 2020/04/18. DOI: 10.14309/ajg.0000000000000664.

472. Yan D, Zhang X, Chen C, et al. Characteristics of Viral Shedding Time in SARS-CoV-2 Infections: A Systematic Review and Meta-Analysis. *Frontiers in Public Health* 2021; 9: 652842. Systematic Review

Research Support, Non-U.S. Gov't.

473. Hong K, Cao W, Liu Z, et al. Prolonged presence of viral nucleic acid in clinically recovered COVID-19 patients was not associated with effective infectiousness. *Emerg Microbes Infect* 2020: 1-26. 2020/09/29. DOI: 10.1080/22221751.2020.1827983.

474. Wu X, Want Z, He Z, et al. A follow-up study shows no new infections caused by patients with repeat positive of COVID-19 in Wuhan. *medRxiv* 2020; PRE-PRINT.

475. Zhou L, Yao M, Zhang X, et al. Breath-, air- and surface-borne SARS-CoV-2 in hospitals. *J Aerosol Sci* 2020: 105693. 2020/10/21. DOI: 10.1016/j.jaerosci.2020.105693.

476. Shrestha NK, Marco Canosa F, Nowacki AS, et al. Distribution of Transmission Potential During Nonsevere COVID-19 Illness. *Clin Infect Dis* 2020; 71: 2927-2932. 2020/07/01. DOI: 10.1093/cid/ciaa886.

477. Perera R, Tso E, Tsang OTY, et al. SARS-CoV-2 Virus Culture and Subgenomic RNA for Respiratory Specimens from Patients with Mild Coronavirus Disease. *Emerg Infect Dis* 2020; 26 2020/08/05. DOI: 10.3201/eid2611.203219.

478. Singanayagam A, Patel M, Charlett A, et al. Duration of infectiousness and correlation with RT-PCR cycle threshold values in cases of COVID-19, England, January to May 2020. *Euro Surveill* 2020; 25 2020/08/15. DOI: 10.2807/1560-7917.ES.2020.25.32.2001483.

479. Bullard J, Dust K, Funk D, et al. Predicting infectious SARS-CoV-2 from diagnostic samples. *Clin Infect Dis* 2020 2020/05/23. DOI: 10.1093/cid/ciaa638.

480. Basile K, McPhie K, Carter I, et al. Cell-based culture of SARS-CoV-2 informs infectivity and safe de-isolation assessments during COVID-19. *medRxiv* 2020; PRE-PRINT.

481. Folgueira MD, Luczkowiak J, Lasala F, et al. Persistent SARS-CoV-2 resplication in severe COVID-19. *MedRxiv* 2020; PREPRINT.

482. Gniazdowski V, Morris CP, Wohl S, et al. Repeat COVID-19 molecular testing: correlation with recovery of infectious virus, molecular assay cycle thresholds, and analytical sensitivity. *medRxiv* 2020; PRE-PRINT.

483. L'Hullier AG, Torriani G, Pigny F, et al. Culture-compentent SARS-CoV-2 in nasopharynx of symptomatic neonates, children, and adolescents. *Emerging Infectious Diseases* 2020; 26.

484. La Scola B, Le Bideau M, Andreani J, et al. Viral RNA load as determined by cell culture as a management tool for discharge of SARS-CoV-2 patients from infectious disease wards. *Eur J Clin Microbiol Infect Dis* 2020; 39: 1059-1061. 2020/04/29. DOI: 10.1007/s10096-020-03913-9.

485. Huang CG, Lee KM, Hsiao MJ, et al. Culture-Based Virus Isolation To Evaluate Potential Infectivity of Clinical Specimens Tested for COVID-19. *J Clin Microbiol* 2020; 58 2020/06/11. DOI: 10.1128/JCM.01068-20.

486. Young BE, Ong SWX, Ng LFP, et al. Viral dynamics and immune correlates of COVID-19 disease severity. *Clin Infect Dis* 2020 2020/08/29. DOI: 10.1093/cid/ciaa1280.

487. Manzulli V, Scioscia G, Giganti G, et al. Real Time PCR and Culture-Based Virus Isolation Test in Clinically Recovered Patients: Is the Subject Still Infectious for SARS-CoV2? *J Clin Med* 2021; 10 2021/01/21. DOI: 10.3390/jcm10020309.

488. Public Health England. *Understanding cycle threshold (Ct) in SARS-CoV-2 RT-PCR - a guide for health protection teams*. 28 October 2020 2020.

489. Li Q, Zheng XS, Shen XR, et al. Prolonged shedding of severe acute respiratory syndrome coronavirus 2 in patients with COVID-19. *Emerg Microbes Infect* 2020: 1-28. 2020/11/17. DOI: 10.1080/22221751.2020.1852058.

490. Xu K, Chen Y, Yuan J, et al. Factors associated with prolonged viral RNA shedding in patients with COVID-19. *Clin Infect Dis* 2020 2020/04/10. DOI: 10.1093/cid/ciaa351.

491. Lan L, Xu D, Ye G, et al. Positive RT-PCR Test Results in Patients Recovered From COVID-19. *JAMA* 2020 2020/02/28. DOI: 10.1001/jama.2020.2783.

492. Song R, Han B, Song M, et al. Clinical and epidemiological features of COVID-19 family clusters in Beijing, China. *J Infect* 2020 2020/04/27. DOI: 10.1016/j.jinf.2020.04.018.

493. Su JW, Wu WR, Lang GJ, et al. Transmission risk of patients with COVID-19 meeting discharge criteria should be interpreted with caution. *J Zhejiang Univ Sci B* 2020; 21: 408-410. 2020/05/20. DOI: 10.1631/jzus.B2000117.

494. Arons MM, Hatfield KM, Reddy SC, et al. Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility. *N Engl J Med* 2020 2020/04/25. DOI: 10.1056/NEJMoa2008457.

495. Kim GU, Kim MJ, Ra SH, et al. Clinical characteristics of asymptomatic and symptomatic patients with mild COVID-19. *Clin Microbiol Infect* 2020 2020/05/04. DOI: 10.1016/j.cmi.2020.04.040.

496. Nissen K, Hagbom M, Krambrich J, et al. Presymptomatic viral shedding and infective ability of SARS-CoV-2; a case report. *Heliyon* 2021; 7: e06328. 2021/03/02. DOI: 10.1016/j.heliyon.2021.e06328.

497. Samaddar A, Gadepalli R, Nag VL, et al. Viral Ribonucleic Acid Shedding and Transmission Potential of Asymptomatic and Paucisymptomatic Coronavirus Disease 2019 Patients. *Open Forum Infect Dis* 2021; 8: ofaa599. 2021/01/29. DOI: 10.1093/ofid/ofaa599.

498. Kawasuji H, Takegoshi Y, Kaneda M, et al. Transmissibility of COVID-19 depends on the viral load around onset in adult and symptomatic patients. *PLoS One* 2020; 15: e0243597. 2020/12/10. DOI: 10.1371/journal.pone.0243597.

499. Yang R, Gui X and Xiong Y. Patients with respiratory symptoms are at greater risk of COVID-19 transmission. *Respir Med* 2020; 165: 105935. 2020/04/21. DOI: 10.1016/j.rmed.2020.105935.

500. ECDC. *Guidance for discharge and ending isolation in the context of widespread community transmission of COVID-19 - first update (8 April 2020)*. 8 April 2020 2020. ECDC.

501. Health Protection Scotland. *Guidance for stepdown of infection control precautions and discharging COVID-19 patients from hospital to residential settings, Version 1.61*. 20 August 2020 2020.

502. Public Health England. *Guidance for stepdown of infection control precautions and discharging COVID-19 patients and asymptomatic SARS-CoV-2 infected patients (22 Mar 2021)*. 22 Mar 2021.

503. Department of Health England and Health Protection Agency. Pandemic (H1N1) 2009 Influenza. Summary infection control guidance for ambulance services during an influenza pandemic. 2009.

504. The Healthcare Infection Control Practices Advisory Committee (HICPAC) and The Centres for Disease Control (CDC). Core Infection Prevention and Control Practices for Safe Healthcare Delivery in All Settings – Recommendations of the Healthcare Infection Control Practices Advisory Committee. 2017.

505. Siegel JD, Rhinehart E, Jackson M, et al. 2007 guideline for isolation precautions: preventing transmission of infectious agents in health care settings. *American Journal of Infection Control* 2007; 35: S65-S164.

506. Leung N, Chu DKW, Shiu E, et al. Respiratory virus shedding in exhaled breath and efficacy of face masks. *Nature Medicine* 2020.

507. Johnson DF, Druce JD, Birch C, et al. A quantitative assessment of the efficacy of surgical and N95 masks to filter influenza virus in patients with acute influenza infection. *Clin Infect Dis* 2009; 49: 275-277. 2009/06/16. DOI: 10.1086/600041.

508. Su WL, Hung PP, Lin CP, et al. Masks and closed-loop ventilators prevent environmental contamination by COVID-19 patients in negative-pressure environments. *J Microbiol Immunol Infect* 2020 2020/05/20. DOI: 10.1016/j.jmii.2020.05.002.

509. Association of periOperative Registered Nurses (AORN). Recommended Practices for Prevention of Transmissible Infections in the Perioperative Practice Setting, (2007).

510. Association for Professionals in Infection control and Epidemiology (APIC), American Nurses Association, Association of Occupational Health Professionals in Healthcare, et al. Do's and don'ts for wearing procedure masks in non-surgical healthcare settings. 2015.

511. Loveday HP, Wilson JA, Pratt RJ, et al. epic3: National Evidence-Based Guidelines for Preventing Healthcare-Associated Infections in NHS Hospitals in England. *Journal of Hospital Infection* 2014; 86: S1-S70.

512. Occupational Safety and Health Administration (OSHA). Guidance on Preparing Workplaces for an Influenza Pandemic. 2009.

513. Gemmell L, Birks R, Radford P, et al. Infection control in anaesthesia. *Anaesthesia* 2008; 63: 1027-1036. Review.

514. Health and Safety Executive. The Control of Substances Hazardous to Health Regulations 2002. 2013.

515. UK Government. The Personal Protective Equipment Regulations 2002. 2002.

516. Coia JE, Ritchie L and Fry C. Use of Respiratory and facial protection. *Nursing Times* 2014; 110: 18-20.

517. Coia JE, Ritchie L, Adisesh A, et al. Guidance on the use of respiratory and facial protection equipment. *Journal of Hospital Infection* 2013; 85: 170-182. Short Survey.

518. Bunyan D, Ritchie L, Jenkins D, et al. Respiratory and facial protection: A critical review of recent literature. *Journal of Hospital Infection* 2013; 85: 165-169. Review.

519. MacIntyre CR, Seale H, Dung TC, et al. A cluster randomised trial of cloth masks compared with medical masks in healthcare workers. *BMJ Open* 2015; 5: e006577. Randomized Controlled Trial Research Support, Non-U.S. Gov't.

520. Health and Safety Executive. *Respiratory protection equipment at work. A practical guide*. 2013.

521. Offeddu V, Yung CF, Low MSF, et al. Effectiveness of Masks and Respirators Against Respiratory Infections in Healthcare Workers: A Systematic Review and Meta-Analysis. *Clin Infect Dis* 2017; 65: 1934-1942. 2017/11/16. DOI: 10.1093/cid/cix681.

522. Seto WH, Tsang D, Yung RW, et al. Effectiveness of precautions against droplets and contact in prevention of nosocomial transmission of severe acute respiratory syndrome (SARS). *Lancet* 2003; 361: 1519-1520. 2003/05/10. DOI: 10.1016/s0140-6736(03)13168-6.

523. Bartoszko JJ, Farooqi MAM, Alhazzani W, et al. Medical Masks vs N95 Respirators for Preventing COVID-19 in Health Care Workers A Systematic Review and Meta-Analysis of Randomized Trials. *Influenza Other Respir Viruses* 2020 2020/04/05. DOI: 10.1111/irv.12745.

524. Greenhalgh T, Chan XH, Khunti K, et al. *What is the efficacy of standard face mask compared to respirator masks in preventing COVID-type respiratory illnesses in primary care staff?* 30 March 2020 2020. Oxford COVID-19 Evidence Service Team.

525. Verbeek JH, Rajamaki B, Ijaz S, et al. Personal protective equipment for preventing highly infectious diseases due to exposure to contaminated body fluids in healthcare staff. *Cochrane Database Syst Rev* 2020; 4: CD011621. 2020/04/16. DOI: 10.1002/14651858.CD011621.pub4.

526. World Health Organization. Infection prevention and control during health care when coronavirus disease (COVID-19) is suspected or confirmed: interim guidance, 29 June 2020. 29 June 2020 2020.

527. Australian Government. Recommended minimum requirements for the use of masks or respirators by health and residential care workers in areas with significant community transmission of COVID-19. 23 October 2020 2020.

528. Government of Canada. Infection prevention and control for COVID-19: Interim guidance for acute healthcare settings. 8 January 2021 2021.

529. Australian Government. Infection Control Expert Group - The use of face masks and respirators in the context of COVID-19, Version 4.0. 11 March 2021 2021.

530. Centers for Disease Control and Prevention. Interim infection prevention and control recommendations for heatlhcare personnel during the Coronavirus Disease 2019 (COVID-19) pandemic - 10 February 2021. 10 February 2021. 2021.

531. Cappa C, Asadi S, Barreda S, et al. Expiratory aerosol particle escape from surgical masks due to imperfect sealing. Research Square 2021; PRE-PRINT/NOT PEER REVIEWED.

532. Ueki H, Furusawa Y, Iwatsuki-Horimoto K, et al. Effectiveness of Face Masks in Preventing Airborne Transmission of SARS-CoV-2. mSphere 2020; 5 2020/10/23. DOI: 10.1128/mSphere.00637-20.

533. Scottish Government. COVID-19: Interim guidance on the extended use of medical masks and face coverings in hospitals and care homes V2.0. 18 September 2020 2020.

534. Lindsley WG, Blachere FM, Law BF, et al. Efficacy of face masks, neck gaiters and face shields for reducing the expulsion of simulated cough-generated aerosols. MedRxiv 2020; PRE-PRINT (NOT PEER-REVIEWED).

535. HSE/ National Health Library and Knowledge Service Evidence Team. What is the current evidence for the effectiveness of using a visor rather than a surgical face mask in preventing the transmission of COVID-19 in a healthcare setting? 14 September 2020 2020. HSE.

536. Health Protection Scotland. National Infection Prevention and Control Manual - Chapter 2 (Trasmission-based precautions). Accessed 13 March 2020 2020. Health Protection Scotland.

537. Australian Government. Guidance on the minimum recommendations for the use of personal protective equipment (PPE) in hospitals during the COVID-19 outbreak, Version 9.0. 9 November 2020 2020.

538. World Health Organization. Coronavirus disease (COVID-19): Masks - Q & A 9 October 2020 2020.

539. ECDC. Using face masks in the community - Reducting COVID-19 transmission from potentially asymptomatic or pre-symptomatic people through the use of face masks. 8 April 2020. 8 April 2020 2020.

540. Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19) - Healthcare Workers - Personal protective equipment Questions and Answers. 8 August 2020 2020.

541. Xu K, Zhang XH, Long XB, et al. An environmental study of tracheostomy on eight COVID-19 patients. J Otolaryngol Head Neck Surg 2021; 50: 3. 2021/01/20. DOI: 10.1186/s40463-021-00494-1.

542. Health and Safety Executive. Rapid review evidence - Delivered by HSE for the Government Chief Scientific Adviser - Part one: equivalence of N95 and FFP2 masks, Part two: aprons, gowns and eye protection. 24 March 2021 2021.

543. Public Health England. COVID-19: infection prevention and control. 2 April 2020 2020.

544. Public Health England. COVID-19: Guidance for the remobilisation of services within health and care settings. Infection prevention and control recommendations. Version 1.0. 20 August 2020 2020.

545. Public Health England. COVID-19: Guidance for maintaining services within health and care settings. Infection prevention and control recommendations, Verson 1.1. . 21 January 2021. 2021.

546. ECRI. Safety of extended use and reuse of N95 respirators - Clinical evidence assessment. March 2020 2020. ECRI.

547. Ozog DM, Sexton JZ, Narla S, et al. The Effect of Ultraviolet C Radiation Against Different N95 Respirators Inoculated with SARS-CoV-2. Int J Infect Dis 2020 2020/09/07. DOI: 10.1016/j.ijid.2020.08.077.

548. Bedell K, Buchaklian AH and Perlman S. Efficacy of an Automated Multiple Emitter Whole-Room Ultraviolet-C Disinfection System Against Coronaviruses MHV and MERS-

CoV. Infect Control Hosp Epidemiol 2016; 37: 598-599. 2016/01/29. DOI: 10.1017/ice.2015.348.

549. Hamzavi IH, Lyons AB, Kohli I, et al. Ultraviolet germicidal irradiation: possible method for respirator disinfection to facilitate reuse during COVID-19 pandemic. J Am Acad Dermatol 2020 2020/04/05. DOI: 10.1016/j.jaad.2020.03.085.

550. Mills D, Harnish DA, Lawrence C, et al. Ultraviolet germicidal irradiation of influenza-contaminated N95 filtering facepiece respirators. Am J Infect Control 2018; 46: e49-e55. 2018/04/22. DOI: 10.1016/j.ajic.2018.02.018.

551. van Straten B, de Man P, van den Dobbelsteen J, et al. Sterilization of disposable face masks by means of standardized dry and steam sterilization processes; an alternative in the fight against mask shortages due to COVID-19. Journal of Hospital Infection 2020; Pre-proof.

552. Daeschler SC, Manson N, Joachim K, et al. Effect of moist heat reprocessing of N95 respirators on SARS-CoV-2 inactivation and respirator function. CMAJ 2020 2020/08/01. DOI: 10.1503/cmaj.201203.

553. Bergman M, Viscusi D, Heimbuch BK, et al. Evaluation of Multiple (3-Cycle) Decontamination Processing for Filtering Facepiece Respirators. 2010 2020; 5.

554. Cadnum JL, Li DF, Redmond SN, et al. Effectiveness of Ultraviolet-C Light and a High-Level Disinfection Cabinet for Decontamination of N95 Respirators. Pathog Immun 2020; 5: 52-67. 2020/05/05. DOI: 10.20411/pai.v5i1.372.

555. Fischer RJ, Morris DH, van Doremalen N, et al. Effectiveness of N95 Respirator Decontamination and Reuse against SARS-CoV-2 Virus. Emerg Infect Dis 2020; 26 2020/06/04. DOI: 10.3201/eid2609.201524.

556. ECDC. Infection prevention and control and preparedness for COVID-19 in healthcare settings. Second update - 31 March 2020. 2020.

557. MacIntyre CR, Wang Q, Cauchemez S, et al. A cluster randomized clinical trial comparing fit-tested and non-fit-tested N95 respirators to medical masks to prevent respiratory virus infection in health care workers. Influenza Other Respir Viruses 2011; 5: 170-179. 2011/04/12. DOI: 10.1111/j.1750-2659.2011.00198.x.

558. World Health Organization. Rational use of personal protective equipment for coronavirus disease 2019 (COVID-19) -Interim Guidance. 27 February 2020 2020. World Health Organization.

559. Kratzel A, Todt D, V'Kovski P, et al. Inactivation of Severe Acute Respiratory Syndrome Coronavirus 2 by WHO-Recommended Hand Rub Formulations and Alcohols. Emerg Infect Dis 2020; 26 2020/04/15. DOI: 10.3201/eid2607.200915.

560. Leslie RA, Zhou SS and Macinga DR. Inactivation of SARS-CoV-2 by commercially available alcohol-based hand sanitizers. Am J Infect Control 2020 2020/08/21. DOI: 10.1016/j.ajic.2020.08.020.

561. Rabenau HF, Kampf G, Cinatl J, et al. Efficacy of various disinfectants against SARS coronavirus. J Hosp Infect 2005; 61: 107-111. 2005/06/01. DOI: 10.1016/j.jhin.2004.12.023.

562. Ong SWX, Tan YK, Chia PY, et al. Air, Surface Environmental, and Personal Protective Equipment Contamination by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) From a Symptomatic Patient. JAMA 2020 2020/03/05. DOI: 10.1001/jama.2020.3227.

563. Ye G, Lin H, Chen S, et al. Environmental contamination of SARS-CoV-2 in healthcare premises. J Infect 2020 2020/05/04. DOI: 10.1016/j.jinf.2020.04.034.

564. Nelson A, Kassimatis J, Estoque J, et al. Environmental Detection of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) from Medical Equipment in Long-Term Care Facilities undergoing COVID-19 Outbreaks. Am J Infect Control 2020 2020/07/10. DOI: 10.1016/j.ajic.2020.07.001.

565. Redmond SN, Dousa KM, Jones LD, et al. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Nucleic Acid Contamination of Surfaces on a Coronavirus Disease 2019 Ward and Intensive Care Unit. Infect Control Hosp Epidemiol 2020: 1-13. 2020/08/13. DOI: 10.1017/ice.2020.416.

566. Zhang S, Wang C, Lin M, et al. Analysis of the Virus Contamination and Disinfection Effect in Isolation Ward of Patients With COVID-19. Front Public Health 2020; 8: 486. 2020/09/29. DOI: 10.3389/fpubh.2020.00486.

567. Hu X, Ni W, Wang Z, et al. The distribution of SARS-CoV-2 contamination on the environmental surfaces during incubation period of COVID-19 patients. Ecotoxicol Environ Saf 2020; 208: 111438. 2020/10/12. DOI: 10.1016/j.ecoenv.2020.111438.

568. Ong SWX, Lee PH, Tan YK, et al. Environmental contamination in a COVID-19 intensive care unit (ICU) - what is the risk? Infect Control Hosp Epidemiol 2020: 1-28. 2020/10/22. DOI: 10.1017/ice.2020.1278.

569. Lomont A, Boubaya M, Khamis W, et al. Environmental contamination related to SARS-CoV-2 in ICU patients. ERJ Open Res 2020; 6 2020/12/02. DOI: 10.1183/23120541.00595-2020.

570. Elbadawy HM, Khattab A, Alalawi A, et al. The detection of SARS-CoV-2 in outpatient clinics and public facilities during the COVID-19 pandemic. J Med Virol 2021 2021/01/28. DOI: 10.1002/jmv.26819.

571. Shah MR, Jan I, Johns J, et al. SARS-CoV-2 nosocomial infection: Real-world results of environmental surface testing from a large tertiary cancer center. Cancer 2021 2021/02/19. DOI: 10.1002/cncr.33453.

572. Hinz A, Xing LY, Doukhanine E, et al. SARS-CoV-2 Detection from the Built Environment and Wastewater and Its Use for Hospital Surveillance. (2021).

573. Peyrony O, Ellouze S, Fontaine JP, et al. Surfaces and equipment contamination by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the emergency department at a university hospital. Int J Hyg Environ Health 2020; 230: 113600. 2020/08/18. DOI: 10.1016/j.ijheh.2020.113600.

574. Colaneri M, Seminari E, Novati S, et al. Severe acute respiratory syndrome coronavirus 2 RNA contamination of inanimate surfaces and virus viability in a health care emergency unit. Clin Microbiol Infect 2020 2020/05/26. DOI: 10.1016/j.cmi.2020.05.009.

575. Ryu BH, Cho Y, Cho OH, et al. Environmental contamination of SARS-CoV-2 during the COVID-19 outbreak in South Korea. Am J Infect Control 2020 2020/06/03. DOI: 10.1016/j.ajic.2020.05.027.

576. Lee SE, Lee DY, Lee WG, et al. Detection of Novel Coronavirus on the Surface of Environmental Materials Contaminated by COVID-19 Patients in the Republic of Korea. Osong Public Health Res Perspect 2020; 11: 128-132. 2020/06/13. DOI: 10.24171/j.phrp.2020.11.3.03.

577. Cheng VC, Wong SC, Chan VW, et al. Air and environmental sampling for SARS-CoV-2 around hospitalized patients with coronavirus disease 2019 (COVID-19). Infect Control Hosp Epidemiol 2020: 1-32. 2020/06/09. DOI: 10.1017/ice.2020.282.

578. Jiang FC, Jiang XL, Wang ZG, et al. Detection of Severe Acute Respiratory Syndrome Coronavirus 2 RNA on Surfaces in Quarantine Rooms. Emerg Infect Dis 2020; 26 2020/05/19. DOI: 10.3201/eid2609.201435.

579. Harvey AP, Fuhrmeister ER, Cantrell M, et al. Longitudinal monitoring of SARS-CoV-2 RNA on high-touch surfaces in a community setting. medRxiv 2020 2020/11/04. DOI: 10.1101/2020.10.27.20220905.

580. Chan KH, Sridhar S, Zhang RR, et al. Factors affecting stability and infectivity of SARS-CoV-2. J Hosp Infect 2020 2020/07/12. DOI: 10.1016/j.jhin.2020.07.009.

581. Kampf G, Todt D, Pfaender S, et al. Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. Journal of Hospital Infection 2020. Review.

582. Booth TF, Kournikakis B, Bastien N, et al. Detection of airborne severe acute respiratory syndrome (SARS) coronavirus and environmental contamination in SARS outbreak units. J Infect Dis 2005; 191: 1472-1477. 2005/04/06. DOI: 10.1086/429634.

583. Dowell SF, Simmerman JM, Erdman DD, et al. Severe acute respiratory syndrome coronavirus on hospital surfaces. Clin Infect Dis 2004; 39: 652-657. 2004/09/10. DOI: 10.1086/422652.

584. Chan KH, Peiris JS, Lam SY, et al. The Effects of Temperature and Relative Humidity on the Viability of the SARS Coronavirus. Adv Virol 2011; 2011: 734690. 2012/02/09. DOI: 10.1155/2011/734690.

585. Biryukov J, Boydston JA, Dunning RA, et al. Increasing Temperature and Relative Humidity Accelerates Inactivation of SARS-CoV-2 on Surfaces. mSphere 2020; 5 2020/07/03. DOI: 10.1128/mSphere.00441-20.

586. Morris DH, Yinda KC, Gamble A, et al. The effect of temperature and humidity on the stability of SARS-CoV-2 and other enveloped viruses. BioRxiv 2020; NOT PEER REVIEWED.

587. Kwon T, Gaudreault NN and Richt JA. Environmental stability of sars-cov-2 on different types of surfaces under indoor and seasonal climate conditions. Pathogens 2021; 10: 1-8.

588. Ronca SE, Sturdivant RX, Barr KL, et al. SARS-CoV-2 Viability on 16 Common Indoor Surface Finish Materials. Herd 2021: 1937586721991535.

589. Paton S, Spencer A, Garratt I, et al. Persistence of SARS-CoV-2 virus and viral RNA on hydrophobic and hydrophilic surfaces and investigating contamination concentration. bioRxiv 2021: 2021.2003.2011.435056. DOI: 10.1101/2021.03.11.435056.

590. Gidari A, Sabbatini S, Bastianelli S, et al. SARS-CoV-2 Survival on Surfaces and the Effect of UV-C Light. Viruses 2021; 13. DOI: 10.3390/v13030408.

591. van Doremalen N, Bushmaker T, Morris DH, et al. Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. N Engl J Med 2020 2020/03/18. DOI: 10.1056/NEJMc2004973.

592. Pastorino B, Touret F, Gilles M, et al. Prolonged Infectivity of SARS-CoV-2 in Fomites. Emerg Infect Dis 2020; 26 2020/06/25. DOI: 10.3201/eid2609.201788.

593. Warnes SL, Little ZR and Keevil CW. Human Coronavirus 229E Remains Infectious on Common Touch Surface Materials. mBio 2015; 6: e01697-01615. 2015/11/12. DOI: 10.1128/mBio.01697-15.

594. Pottage T, Garratt I, Onianwa O, et al. A Comparison of Persistence of SARS-CoV-2 Variants on Stainless Steel. bioRxiv 2021: 2021.2004.2008.438833. DOI: 10.1101/2021.04.08.438833.

595. Riddell S, Goldie S, Hill A, et al. The effect of temperature on persistence of SARS-CoV-2 on common surfaces. Virol J 2020; 17: 145. 2020/10/09. DOI: 10.1186/s12985-020-01418-7.

596. Carducci A, Federigi I, Liu D, et al. Making Waves: Coronavirus detection, presence and persistence in the water environment: State of the art and knowledge needs for public health. Water Res 2020; 179: 115907. 2020/05/12. DOI: 10.1016/j.watres.2020.115907.

597. Gundy P, Gerba C and Pepper I. Survival of coronaviruses in water and wastewater. Food and Environmental Virology 2009; 1: 10.

598. Wang J, Feng H, Zhang S, et al. SARS-CoV-2 RNA detection of hospital isolation wards hygiene monitoring during the Coronavirus Disease 2019 outbreak in a Chinese hospital. Int J Infect Dis 2020; 94: 103-106. 2020/04/21. DOI: 10.1016/j.ijid.2020.04.024.

599. Ge T, Lu Y, Zheng S, et al. Evaluation of disinfection procedures in a designated hospital for COVID-19. Am J Infect Control 2020 2020/08/26. DOI: 10.1016/j.ajic.2020.08.028.

600. Medema G, Heijnen L, Elsinga G, et al. Presence of SARS-Coronavirus-2 in sewage. medRxiv 2020; PRE-PRINT. DOI: **https://doi.org/10.1101/2020.03.29.20045880**

601. Wu FQ, Xiao A, Zhang JB, et al. SARS-CoV-2 titers in wastewater are higher than expected from clinically confirmed cases. medRxiv 2020; PRE-PRINT. DOI: **https://doi.org/10.1101/2020.04.05.20051540**.

602. Nemudryi A, Nemudraia A, Surya K, et al. Temporal detection and phylogenetic assessment of SARS-CoV-2 in municipal wastewater. medRxiv 2020; PRE-PRINT. DOI: **https://doi.org/10.1101/2020.04.15.20066746**.

603. Wurtzer S, Marechal V, Mouchel J, et al. Evaluation of lockdown impact on SARS-CoV-2 dynamics through viral genome quantification in Paris wastewaters. medRxiv 2020; PRE-PRINT. DOI: **https://doi.org/10.1101/2020.04.12.20062679**

604. Randazzo W, Cuevas-Ferrando E, Sanjuan R, et al. Metropolitan wastewater analysis for COVID-19 epidemiological surveillance. Int J Hyg Environ Health 2020; 230: 113621. 2020/09/11. DOI: 10.1016/j.ijheh.2020.113621.

605. Crits-Christoph A, Kantor RS, Olm MR, et al. Genome sequencing of sewage detects regionally prevalent SARS-CoV-2 variants. MedRxiv 2020; PREPRINT.

606. Peccia J, Zulli A, Brackney DE, et al. Measurement of SARS-CoV-2 RNA in wastewater tracks community infection dynamics. Nat Biotechnol 2020 2020/09/20. DOI: 10.1038/s41587-020-0684-z.

607. Martin J, Klapsa D, Wilton T, et al. Tracking SARS-CoV-2 in Sewage: Evidence of Changes in Virus Variant Predominance during COVID-19 Pandemic. Viruses 2020; 12 2020/10/15. DOI: 10.3390/v12101144.

608. D'Aoust PM, Graber TE, Mercier E, et al. Catching a resurgence: Increase in SARS-CoV-2 viral RNA identified in wastewater 48 h before COVID-19 clinical tests and 96 h before hospitalizations. Sci Total Environ 2021; 770: 145319. 2021/01/29. DOI: 10.1016/j.scitotenv.2021.145319.

609. Wade M, Jones D, Singer A, et al. Wastewater COVID-19 monitoring in the UK: summary for SAGE - 19/11/20. 19 November 2020 2020. UK Government.

610. Emergencies SAGf. Eighty-sixth SAGE meeting on COVID-19, 08 April 2021. 2021.

611. Jahn K, Dreifuss D, Topolsky I, et al. Detection of SARS-CoV-2 variants in Switzerland by genomic analysis of wastewater samples. . MedRxiv 2021; PREPRINT.

612. La Rosa G, Bonadonna L, Lucentini L, et al. Coronavirus in water environments: Occurrence, persistence and concentration methods - A scoping review. Water Res 2020; 179: 115899. 2020/05/04. DOI: 10.1016/j.watres.2020.115899.

613. Geller C, Varbanov M and Duval RE. Human coronaviruses: insights into environmental resistance and its influence on the development of new antiseptic strategies. Viruses 2012; 4: 3044-3068. 2012/12/04. DOI: 10.3390/v4113044.

614. Gerlach M, Wolff S, Ludwig S, et al. Rapid SARS-CoV-2 Inactivation by Commonly Available Chemicals on Inanimate Surfaces. J Hosp Infect 2020 2020/09/12. DOI: 10.1016/j.jhin.2020.09.001.

615. Xiling G, Yin C, Ling W, et al. In vitro inactivation of SARS-CoV-2 by commonly used disinfection products and methods. Sci Rep 2021; 11: 2418. 2021/01/30. DOI: 10.1038/s41598-021-82148-w.

616. Welch SR, Davies KA, Buczkowski H, et al. Analysis of Inactivation of SARS-CoV-2 by Specimen Transport Media, Nucleic Acid Extraction Reagents, Detergents, and Fixatives. J Clin Microbiol 2020; 58 2020/08/26. DOI: 10.1128/JCM.01713-20.

617. The US Centers for Disease Control & Prevention. Science Brief: SARS-CoV-2 and Surface (Fomite) Transmission for Indoor Community Environments. 5th April 2021 2021.

618. Reed NG. The history of ultraviolet germicidal irradiation for air disinfection. Public Health Rep 2010; 125: 15-27. 2010/04/21. DOI: 10.1177/003335491012500105.

619. Kovach CR, Taneli Y, Neiman T, et al. Evaluation of an ultraviolet room disinfection protocol to decrease nursing home microbial burden, infection and hospitalization rates. BMC Infect Dis 2017; 17: 186. 2017/03/04. DOI: 10.1186/s12879-017-2275-2.

620. Jureka AS, Williams CG and Basler CF. Pulsed Broad-Spectrum UV Light Effectively Inactivates SARS-CoV-2 on Multiple Surfaces and N95 Material. Viruses 2021; 13: 11.

621. Kitagawa H, Nomura T, Nazmul T, et al. Effectiveness of 222-nm ultraviolet light on disinfecting SARS-CoV-2 surface contamination. Am J Infect Control 2020 2020/09/09. DOI: 10.1016/j.ajic.2020.08.022.

622. Heilingloh CS, Aufderhorst UW, Schipper L, et al. Susceptibility of SARS-CoV-2 to UV Irradiation. Am J Infect Control 2020 2020/08/09. DOI: 10.1016/j.ajic.2020.07.031.

623. Bianco A, Biasin M, Pareschi G, et al. UV-C irradiation is highly effective in inactivating and inhibiting SARS-CoV-2 replication. MedRxiv 2020; NOT PEER-REVIEWED.

624. Simmons SE, Carrion R, Alfson KJ, et al. Deactivation of SARS-CoV-2 with pulsed-xenon ultraviolet light: Implications for environmental COVID-19 control. Infect Control Hosp Epidemiol 2020: 1-4. 2020/08/04. DOI: 10.1017/ice.2020.399.

625. Inagaki H, Saito A, Sugiyama H, et al. Rapid inactivation of SARS-CoV-2 with deep-UV LED irradiation. Emerg Microbes Infect 2020; 9: 1744-1747. 2020/07/17. DOI: 10.1080/22221751.2020.1796529.

626. Criscuolo E, Diotti RA, Ferrarese R, et al. Fast inactivation of SARS-CoV-2 by UV-C and ozone exposure on different materials. Emerg Microbes Infect 2021; 10: 206-210. 2021/01/06. DOI: 10.1080/22221751.2021.1872354.

627. Health Protection Scotland. Literature review and practice recommendations: existing and emerging technologies used for decontamination of the healthcare environment - Ultraviolet Light. 2016. Health Protection Scotland,.