Rapid Review of the literature: Assessing the infection prevention and control measures for the prevention and management of COVID-19 in healthcare settings

Version: 1.1

Date: 3 April 2020

Contents

Abbreviations

ABHR	Alcohol based hand rub
AGP	Aerosol-generating procedure
FFP2	Filtering face piece respirator (class 2)
FFP3	Filtering face piece respirator (class 3)
FRSM	Fluid-resistant surgical face mask
HDU	High dependency unit
ICU	Intensive care unit
ITU	Intensive therapy unit
MERS-CoV	Middle East respiratory syndrome coronavirus
NIPCM	National Infection Prevention and Control Manual
NERVTAG	New and Emerging Respiratory Virus Threat Assessment Group
PPE	Personal protective equipment
RPE	Respiratory protective equipment
SARS-CoV	Severe acute respiratory syndrome coronavirus
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
WHO	World Health Organization

1. Aim

To provide a rapid review of the scientific evidence base to determine if the infection prevention and control measures applied in Scotland are suitable for the prevention and management of COVID-19 in healthcare settings.

2. Objectives

Objectives for the rapid review were to establish the following:

- The routes of transmission;
- The incubation period;
- The infectious period;
- The environmental survivability of the SARS-CoV-2;
- The methods for cleaning/decontamination of the care environment;
- The personal protection equipment (PPE) requirements;
- The respiratory protection equipment (RPE) requirements;
- The methods of hand hygiene.

3. Search Strategy

Academic databases were searched on 5th March 2020 to identify relevant literature and additional hand searching was conducted.

The search terms 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. surgical mask?.mp.
13. hand hygiene.mp.
14. clean*.mp.
15. transmission.mp.
16. 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15
17. 6 and 16
18. limit 17 to English language
19. limit 18 to yr="2020 -Current"

Evidence updates

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

Results

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. Most papers highlight the need for further research, with existing SARS-CoV and MERS-CoV knowledge filling current gaps where appropriate.

4. Transmission routes

The transmission of COVID-19 is thought to occur mainly through respiratory droplets generated by coughing and sneezing, and through contact with contaminated surfaces. Preliminary evidence indicates the routes of transmission to be droplet[1-10] and contact.[1, 3, 6-11] Evidence also supports indirect contact.[1, 6, 7, 9, 10] These transmission routes are supported by National[12-14] and international guidance.[15, 16]

Currently there is no clear evidence of airborne transmission of SARS-CoV-2. Aerosol-generating procedures (AGPs) have been associated with an increased risk of transmission of previous coronaviruses (SARS-CoV and MERS-CoV)[16] and a number of AGPs (mostly airway management) have been implicated as risk factors for SARS-CoV-2.[9] Therefore airborne precautions should be put in place for all AGPs performed on suspected/confirmed COVID-19 patients.

Analysis of 53,000 confirmed cases found that 7.7% experienced gastrointestinal symptoms, with approximately 5.7% experiencing diarrhoea.[17] Initial reports from mainland China suggest that nausea and vomiting are also infrequently reported (5.0% of 1099 confirmed cases).[18] A number of papers cited the need for more research into the possibility of faecal-oral transmission[2, 6, 7, 9-11, 19, 20] following the discovery of viral RNA in the stool samples of COVID-19 patients.[21-24] The majority of studies report on single patient cases[21, 22, 24, 25] and/or lack robust clinical data[21, 23] (i.e. time course of illness, incubation period) which limits interpretation of the epidemiological significance of clinical samples. To date there is no evidence of direct human-to-human transmission from faecal material. The transmission risk from non-respiratory samples is still being investigated; initial attempts at live virus isolation from stool have been unsuccessful.[26] 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. 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.[26] 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.

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.[23, 27] 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.

SARS-CoV-2 has been detected in the tears and conjunctival secretions in COVID-19 patients with conjunctivitis[4] leading to the suggestion that transmission could be possible via the mucous membranes of the eyes.[28, 29] All secretions (except sweat) and excretions from patients with known or suspected COVID-19, should therefore be regarded as potentially infectious.

There is limited evidence regarding mother-to-child transmission. A small study investigating delivery via caesarean section found no evidence of vertical transmission in pregnant women who developed COVID-19 pneumonia in the third trimester however further research is needed.[30]

Atypical presentations

Atypical presentations include cases that do not display the typical respiratory symptoms or fever (which constituted the case definition to date) but may test positive or show radiographic abnormalities (i.e. ground-glass opacity). Chan et al describe a family cluster of cases that included a 10 year old asymptomatic child (nil respiratory symptoms or fever) that tested positive from respiratory samples and had ground-glass opacity on radiography. There was no evidence that this patient contributed to transmission. An atypical presentation occurred in an Italian national evacuated from China and quarantined on arrival with 56 others as a precautionary measure.[25] 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. No transmission events from this case were reported. 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.[31] Again, no transmission events were reported from these patients. 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:

- Standard Infection Control Precautions (SICPs) should be applied at all times regardless of the infectious nature of the patient.

- Droplet precautions should be implemented when in close contact (up to 2 metres) with, or providing direct patient care of, a suspected/confirmed COVID-19 patient.
- Airborne precautions should be implemented when undertaking an AGP. See Appendix 16 of the NIPCM for more information.

5. Incubation period

Early reports vary regarding the incubation period and 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 to date suggests an incubation period of 5-6 days[7, 10, 32-42] with a range of 1-14 days[7, 8, 11, 18, 35, 37, 39, 40, 43, 44] from infection to symptoms surfacing. 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), 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.[34]

Conclusion:

- The incubation period for most people is 5-6 days (range 1-14 days).
- Self-isolation for 7 days is recommended for individuals with symptoms consistent with COVID-19.
- Self-isolation for 14 days is recommended for contacts of symptomatic cases.

6. Infectious period

Assessment of the clinical and epidemiological characteristics of SARS-CoV-2 cases suggests that, similar to SARS-CoV, patients are not infectious until the onset of symptoms.[35] 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 hospitalized therefore the proportion of milder community cases may be underestimated.[35]

Less is known about the duration of infectivity. The presence of viral RNA may not represent transmissible infectious viral cells. From limited international data, the balance of evidence is that, for mild cases of infection, infectivity (as determined by clinical sampling) significantly reduces 7 days after the onset of symptoms but appears to take longer for severe cases.[26, 35, 45] 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.[26] 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.[26] 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 single study suggests that as viral load reduces in the later stages of infection, so too does transmission risk. 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.[26] Further research is required in the area of viral isolation to develop a robust evidence base.

Asymptomatic transmission

Viral RNA can be detected in clinical samples post symptom resolution which has prompted fears of asymptomatic transmission however the actual risk of transmission in these situations is unknown. Reports that suggest possible infectivity are based on limited evidence from (largely retrospective observations during contact tracing) and identification of viral RNA in clinical samples post symptom resolution.[10, 27, 43, 46-48] Three studies report on identification of viral RNA in clinical samples in asymptomatic patients[27, 46, 47] however only one of these studies provides evidence of possible presymptomatic transmission, occurring in the *incubation period* prior to symptom onset. Rothe et al report a 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.[47] Having developed symptoms on return to China, contact tracing was carried out and two German colleagues were identified as positive with mild symptoms. A recent report details possible presymptomatic transmission in 7 community case clusters in Singapore; date of exposure could be determined in 4 clusters and suggested transmission occurring 1-3 days prior to symptom onset from source patients.[49] Paediatric cases have been reported detailing asymptomatic presentations with positive

clinical samples however transmission events from these cases could not be proven.[27, 46] Such studies are limited by their small sample size and observational nature and often lack robust clinical data. As clinical sampling may not be widely conducted on mild/community-based cases, there may continue to be a paucity of data in relation to determination of asymptomatic transmission. The majority of evidence to date continues to point towards transmission occurring predominantly during the symptomatic period.

Conclusion:

- Transmission is most likely to occur whilst a person is symptomatic.
- In mild cases of infection, the risk of transmission is thought to significantly reduce after 7 days.
- 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 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.

7. Survival in the environment

A recent environmental sampling study of isolation rooms occupied by COVID-19 patients sampled various locations immediately prior to environmental cleaning; virus was found on the bed rail, locker, chair, light switches, sink, floor, window, PPE storage area and air outlet fan, as well as the toilet bowl surface and door handle.[50] This study highlights the potential for environmental contamination, particularly of frequently-touched areas. In light of limited data for SARS-CoV-2 regarding survival time in the environment, evidence was assessed from studies conducted with previous human coronaviruses including MERS-CoV and SARS-CoV. 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, 20, 51-54] Survival is also dependent on the surface type.[51] An experimental study using a SARS-CoV-2 strain reported viability on plastic for up to 72 hours, for 48 hours on stainless steel and up to 8 hours on copper.[55] Viability was quantified by end-point titration on Vero E6 cells.

Conclusion:

- Due to the uncertainty regarding the environmental survivability of SARS-CoV2 in real-life conditions, it is essential to increase the frequency of routine cleaning and ensure that the environment is clutter free.
- Cleaning and disinfection using at least 1000ppm av Cl is required

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.[20, 51, 56] 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.[56] Limited evidence suggests that coronaviruses are susceptible to chlorine-based disinfectants and ethanol-based antiseptics.[51, 57] 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.[51] The World Health Organization (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.[50]

Conclusion:

- Environmental cleaning and disinfection should be carried out in line with the National Infection Prevention and Control Manual (NIPCM).
- This includes: a combined detergent/disinfectant solution at a dilution of 1,000 parts per million available chlorine (ppm available chlorine (av.cl.)) for transmission-based environmental cleaning.[58] Small surfaces can be disinfected with 70% ethanol.

9. Personal protective equipment

There was limited evidence for the assessment of the PPE and RPE requirements for the prevention of transmission of SARS-CoV-2. Determination of the PPE requirements for novel pathogens is usually based on previous experience with similar pathogens and/or similarly-transmitted pathogens. Determination of the efficacy of PPE recommendations is based on retrospective analyses of possible transmission events to healthcare workers, where any associations with PPE worn at the time are assessed. Such assessments are considered to be low quality evidence and prone to confounding. 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 droplet precautions were adequate for prevention of nosocomial SARS where no aerosolisations are expected.[59] The non-infected staff who wore surgical masks and N95 respirators were significantly associated with non-infection but this was not the case for the non-infected staff that wore paper masks. Only 2 of the 13 infected HCWs wore RPE (both paper masks). A similar SARS-CoV case-control found a protective effect of N95 respirators as well as hand-washing following patient contact whereas gown and glove use was not protective.[60] The PPE requirements and indications in this study were gradually heightened in response to the increasing nosocomial spread, with all HCWs wearing N95 respirators for all patient care by the end of the study. Notably there was no significant difference in the distribution of suctioning, intubation and oxygen administration between cases and controls. As is the case for these types of studies, risk of bias and confounding was high as compliance and use of PPE was self-reported.

A systematic review and meta-analysis combining 6 case-control and 3 cohort studies, found that use of RPE 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 indications (and compliance) for mask/respirator use varied between the included studies.[61] It should be noted that N95 respirators (which are the equivalent of FFP2 respirators in terms of filtering efficacy) are not recommended for use in UK healthcare settings. FFP3 respirators should be worn for airborne precautions and when performing AGPs, and must be compliant with EN149:2001 FFP3.

For general patient care (i.e. non-AGP situations), the first edition of the UK IPC pandemic COVID-19 guidance initially recommended FRSMs, disposable aprons and disposable gloves, with the decision to wear eye protection based on risk assessment, and fluid-resistant long sleeve gowns recommended for confirmed cases and all AGPs.[14] 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.[62] The guidance states 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 is not in line with the evidence base to date for COVID-19 as discussed in this rapid review, it is 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 is also a move towards sessional use of PPE in light of the recognised global shortage of PPE stockpiles and perhaps in recognition of the fact that the change in PPE recommendations are likely to result in greater use of PPE by a wider staff group which will deplete existing UK stocks. 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.[63] 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.[63]

Specifically, FRSMs are recommended for direct patient care (within 2 metres) in inpatient, radiology, maternity and labour wards (2nd/3rd stage labour vaginal delivery – no AGPs), operating theatres (no AGPs), emergency departments/acute assessment areas, and when transferring possible (suspected) or confirmed cases.[62] Either a disposable plastic apron or a fluid-resistant gown can be worn, with the exception being when performing AGPs outside high risk acute care areas, when a gown must be worn. Eye protection (single or reusable full face visor or goggles) is recommended at all times with the exception of inpatient care to any individuals in the extremely vulnerable group undergoing shielding.[62]

Conclusion:

- Droplet precautions should be adhered to for general patient care.

- Airborne precautions are required when providing care in high risk units and when performing AGPs on patients with COVID-19.
- Healthcare workers should undertake an individual risk assessment on the need for PPE including sessional use of these items as per UK IPC COVID-19 guidance.

10. Respiratory protection equipment

The Department of Health and Social Care's New and Emerging Respiratory Virus Threat Assessment Group (NERVTAG) recommends 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).

In areas where AGPs are less frequently performed a fluid-resistant (Type IIR) surgical mask (FRSM) is recommended; all general ward staff, community, ambulance and social care staff should wear an FRSM for close patient contact (within 2 metres), unless performing an AGP, when a filtering face piece (class 3) (FFP3) respirator should be worn.

The updated (as of 2nd April 2020) UK IPC pandemic COVID-19 guidance recommends that an FFP3 respirator should be worn when working in higher risk acute care areas (ICU/HDU/ED resuscitation areas/wards with non-invasive ventilation/operating theatres/endoscopy units for upper respiratory, ENT or upper GI endoscopy/any other clinical areas where AGPs are regularly performed), and when performing AGPs in areas outside the aforementioned areas.[62]

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.[58] The UK IPC pandemic COVID-19 guidance also recommends that, in addition to FFP3 respirators and face protection, disposable gloves and long sleeved disposable gowns should be worn when performing AGPs. Similar guidance for COVID-19 PPE for critical care and anaesthesiology teams is provided by Wax et al[9] and in a rapid advice guideline by Jin et al for general patient care[8] (N95 respirators along with full face visors, gowns and overalls).

Conclusion:

- FFP3/2 respirators should be worn at all times in clinical areas considered AGP 'hot spots' such as ICUs, ITUs and HDUs, and in all clinical settings when performing an AGP.
- Fluid-resistant (Type IIR) surgical facemasks should be worn in all other clinical settings (i.e. general wards), and, when entering cohort areas when no patient contact is anticipated.
- Healthcare staff should assess the need for RPE including eye protection and if required wear this on a sessional basis following the UK COVID-19 IPC guidance.

11. Hand hygiene

The majority of articles identified recommend that hand hygiene should be performed, however many do not specify the method(s) to be used in preventing the transmission of SARS-CoV-2. A number of guidance documents provide specific methodologies 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] Rabenau et al provide experimental evidence for the efficacy of commercially-available ABHRs against SARS-CoV and reported deactivation to below the detectable limit within a contact time of 30 seconds.[56] Due to the similarity between SARS-CoV and SARS-CoV-2, it is likely that ABHRs would be effective against both viruses.

Conclusion:

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

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.

. Centres for Disease Control and Prevention,2020, p. https://www.cdc.gov/coronavirus/2019-ncov/about/transmission.html

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

17. 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.

18. 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.

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

20. 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.

21. 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.

22. 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.

23. 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.

24. 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.

25. 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.

26. 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.

27. 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.

28. 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.

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

30. 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.

31. 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.

32. 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).

33. 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.

34. 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.

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

36. 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.

37. 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.

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

39. 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.

40. 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.

41. 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.

42. 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.

43. 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.

44. 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.

45. 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.

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

47. 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.

48. 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.

49. 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.

50. 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.

51. 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.

52. 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.

53. 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.

54. 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.

55. 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.

56. 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.

57. 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.

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

59. 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.

60. Teleman MD, Boudville IC, Heng BH, et al. Factors associated with transmission of severe acute respiratory syndrome among health-care workers in Singapore. *Epidemiol Infect* 2004; 132: 797-803. 2004/10/12. DOI: 10.1017/s0950268804002766.

61. 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.

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

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