



What's in the Pipeline? Evidence on the Transmission of SARS-CoV-2 via Building Wastewater Plumbing Systems

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There is emerging evidence of the transmission of SARS-CoV-2 via the sanitary plumbing wastewater system, a known transmission pathway of SARS-CoV-1. These events can no longer be dismissed as isolated cases, yet a lack of awareness and of basic research makes it impossible to say just how widespread this mode of transmission might be. Virus is transmitted within wastewater systems by the aerosolisation of wastewater and subsequent transport of bioaerosols on naturally occurring airflows within the piped network. Central to the debate around risk to building occupants from SARS-CoV-2 spread via wastewater plumbing systems is the question of infectivity of faeces, urine and associated aerosols. This paper presents an examination of the processes which underlie this mode of transmission, and the existing epidemiological evidence, as well as existing mitigation strategies; significant gaps in the state of the knowledge are also identified. It is hoped that this review will cultivate a wider awareness and understanding of this most overlooked of threats, and to facilitate the selection and adoption of appropriate mitigation strategies. Key gaps in the knowledge span the rate of generation of bioaerosols within the building drainage system, their composition and transport properties, and the viability and infectivity of virions and other pathogens which they carry. While much of this work will be conducted in the laboratory, we also identify a dearth of field observations, without which it is impossible to truly grasp the scale of this problem, its character, or its solution.

Keywords: SARS-CoV-2, buildings, wastewater, plumbing, COVID-19

INTRODUCTION

Concern has been raised that the building drainage system (BDS) may pose a risk of infection of SARS-CoV-2 (Gormley et al., 2020a; Patel, 2020), particularly in tall buildings where drainage systems can be subject to higher air pressures. In the Amoy Gardens SARS-CoV-1 outbreak, a cumulative effect was posited as contributing to spread by this route; the index case is said to have used the toilet "several times" during his visit (Hung et al., 2006), and the large number of flats connected to a common drainage stack would have led to much elevated levels of viral aerosol within the BDS once the outbreak was underway. "Watery diarrhoea", (Choi et al., 2003; Peiris et al., 2003), a common symptom, is believed to have generated a "diarrhoeal mist" in the building drainage system, which served as the vector for the Amoy Gardens outbreak (Gormley et al., 2013). Viral aerosols are believed to have entered other flats through depleted water traps, with "several" having floor-level

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In SARS-CoV-1, diarrhoea was identified on admission in 10.6% (Hung et al., 2004) and 15% (Choi et al., 2003) of patients in two large cohorts in Hong Kong, while Booth et al. (2003) observed it in 23.6% of patients on admission to hospitals across Toronto. Hung et al. (2004) reported diarrhoea in 43.5% of patients during days 10-15 post-admission, while 53% of patients in Choi et al. (2003) developed diarrhoea during the course of the study, at a median of 3 days after admission. Peiris et al. (2003) reported that 73% of patients suffered diarrhoea, at a mean of 7.5 days after onset, and Booth et al. (2003) reported that the median time until onset was 8 days from admission. In SARS-CoV-1, diarrhoea was associated with the elevated presence of viral RNA in stool samples. Hung et al. (2004) reported median values of 10^{7.5}/ml and 10^{5.0}/ml in patients with and without diarrhoea respectively; RNA was present in much lesser concentrations, and in fewer patients (10^{4.4}/ml, 28.2%) in urine. Lau et al. (2005) reported many stool samples with between 108 and 1010 copies/ml of SARS-CoV-1 RNA, with some possibly exceeding these values. At Amoy Gardens, virus-laden aerosol are thought to have entered flats through dry floor drainage traps, driven by positive pressures generated within the system by the flow of wastewater and negative pressures generated by bathroom extract fans (Hung et al., 2006; Jack et al., 2006).

For there to be a similar risk with SARS-CoV-2, viable virus must enter the building drainage system. While at Amoy Gardens this was apparently associated with an index patient with diarrhoea, it has long been known that viable pathogens also diffuse from the stools of asymptomatic patients (Moore et al., 1952; Breathnach et al., 2012). This has been the basis for a substantial body of research, which has widely been translated into practice to monitor the presence of SARS-CoV-2, particularly in pre-symptomatic and asymptomatic populations, by wastewater sampling (Chavarria-Miró et al., 2020; Polo et al., 2020). It must be stressed that although related, this is a quite distinct field of inquiry. In this paper, the emphasis is on the "above-ground" drainage system, and the transmission of disease by the formation and transmission of viable bioaerosols.

One probable instance of the transmission of SARS-CoV-2 *via* the building drainage system has been identified in the peerreviewed literature (Gormley, 2020; Kang et al., 2020), in a 30storey residential building in Guangzhou. The building is served by separate blackwater and greywater stacks which share a common vent pipe. Residents of Flat 1502 had Covid; occupants of Flats 2502 and 2702, on the same drainage stack, subsequently developed Covid, despite stringent social distancing measures. No-one living elsewhere in the building became infected. Interpersonal contact was excluded as a means of transmission, and sampling of common areas, including lifts, did not identify any virus. Virus could not be identified in any of eleven environmental samples taken from Flats 2502 and 2702 shortly after a programme of disinfection. However, a swab comprising material from the washbasin trap, shower switch, and a tap, from the vacant Flat 1602, tested positive. Whereas the use of floor drains drew criticism in the wake of the Amov Gardens outbreak (Hung et al., 2006), interviews here also identified a likelihood of dry bathtub traps. The potential for aerosol spread through the system was tested using a tracer gas injected into the drainage system at the WC discharge of Flat 1502. Bathroom doors and windows were left open, which was justified by interviews with residents; tracer gas was identified in the dry bathtub and floor drain traps of each of the five flats investigated. As in the Amoy Gardens outbreak, it is unclear whether the final transmission might have been airborne, or via fomites such as surfaces or hygiene products (Gormley et al., 2017).

Kang et al. (2020) cite two further likely examples of Covid transmission through the building drainage system in Hong Kong, from outwith the peer-reviewed literature.

LITERATURE REVIEW

We conducted systematic literature reviews to assess the prevalence of diarrhoea in Covid, and the prevalence of SARS-CoV-2 in stool and urine. PubMed and Scopus were searched up to August 31, 2020, with the default settings employed to specify synonyms and alternative spellings, and to search titles, abstracts and key words. Materials in English, French, Spanish and Russian were reviewed, to the exclusion of those in Chinese and Dutch. Titles and abstracts were used to exclude material which was clearly not relevant, with all remaining papers reviewed in full. Where only an abstract was available, this was considered acceptable for review.

Diarrhoea in SARS-CoV-2

The first part of the review addressed the prevalence of diarrhoea in Covid, using the terms (Covid OR SARS-CoV-2) AND (diarrhoea OR loose stool*). This yielded 1181 results, of which 236 were unique to PubMed, 614 were unique to Scopus, and 331 were common to both. The review of titles and abstracts was used to identify cohort studies or non-family case series presenting original research on the symptoms of Covid. 318 papers were reviewed in full, of which 213 met the inclusion criteria for further analysis.

Excluding cohorts of pregnant patients and those with underlying conditions, 89 unique groups were identified, which are presented in **Supplementary Appendix 1** The widely differing rates of diarrhoea reported, and the differences which underlie them, mean that any aggregation of results must be tret with extreme caution, although a reference value derived from the adult studies of 4506/28,180 (16.0%) will be useful for subsequent analysis. Notwithstanding the variations in prevalence reported, a comparison of different studies and groups of studies clarifies the role of diarrhoea in the course of Covid, which is necessary to understand the risk from virus in faeces.

Different studies report on different definitions of diarrhoea, and the definition was not stated in the majority of cases. A minimum of three episodes over the course of a day or other 24 h period is a common requirement (Ellington et al., 2020; Jin et al., 2020; Lo et al., 2020; Shang et al., 2020; Zhang H. et al., 2020), however Xiao Y. et al. (2020) reported that 40 of 63 cases with diarrhoea passed stool 1-3 times/day, and Pan et al. (2020) reported diarrhoea "typically up to thrice daily". Some authors required symptoms to persist for more than 1 day (Ai et al., 2020; Ishiguro et al., 2020), while others reported on shorter manifestations (Jin et al., 2020; Remes-Troche et al., 2020). Whereas the majority of studies used data recorded by healthcare workers, several relied on self-reporting. Menni et al. (2020) gathered symptom and Covid test data in the United Kingdom and United States using an app. Selfreported prevalence of diarrhoea was 509,174/2,600,461 (19.6%) among those not tested for Covid, 2359/11,493 (20.5%) among those with negative test results, and 1913/7178 (26.7%) among those with positive Covid tests. Clemency et al. (2020) recorded diarrhoea in 57/225 (25.3%) healthcare workers asked to self-report who tested positive for Covid, and in 26.1% of those with negative tests. Magnavita et al. (2020) additionally surveyed healthcare workers who were not tested; this control group reported diarrhoea in 15/361 (4.2%) cases, as compared to 13/152 (8.6%) among those who received negative tests, and 20/ 82 (24.4%) of those with positive tests.

In largest cohort included here, Abraham et al. (2020) reported one of the lowest rates of diarrhoea, with 396/22,425 (1.8%) reported to have suffered "loose stools", itself a relatively lenient marker. Although this study included 40,184 Covid cases verified by PCR, symptom status and description were missing in 17,759 cases. The 22,425 cases described comprised patients symptomatic following potential exposure (5727), those hospitalised with severe acute respiratory infections (4204), patients with flu-like symptoms in Covid hotspots (1199), and asymptomatic cases screened due to likely exposure (11,295). The high number of asymptomatic cases here seems likely to indicate an underrepresentation of asymptomatic cases in the other studies reviewed. Although this would suggest that the prevalence of diarrhoea across the entire population of those infected with Covid could be lower than reported elsewhere, there is considerable uncertainty around the figure of 1.8%, with unknowns including the bias among those whose data were missing, the efficiency of the contact tracing system, and how many cases here presented as asymptomatic would go on to develop symptoms. Other studies generally identified asymptomatic patients at much lower levels or not at all, although Magnavita et al. (2020) identified 24 asymptomatic cases among 84 healthcare workers with Covid (29.3%).

The reasons posed above with reference to the literature do not seem to fully account for the extreme variation in values reported. Influences not directly in evidence could include cultural factors leading to over-reporting or underreporting of diarrhoea, particularly but not solely where symptoms are self-reported, and in the absence of a prescribed definition. Socioeconomic conditions also influence patients' readiness to seek medical attention. In addition to factors influencing the reporting of diarrhoea, prior health status affects the prevalence of diarrhoea; the impact of certain underlying health conditions is reviewed below and found to be significant, including in case-control studies. Gayam et al. (2020), who reported diarrhoea among 220/408 (53.9%) patients in a deprived area of New York, cited "prevailing relatively poor health" as likely to have been the major factor behind poor clinical course and prognosis in this cohort.

The Characterisation of Diarrhoea and its Significance

Where initial symptoms were documented across the adult and predominantly adult cohorts, diarrhoea was among them in 24/271 (8.9%) cases; by admission, it had developed in 7404/60,205 (12.3%) cases; several studies provided more description, demonstrating the development of diarrhoea at various times during the disease course, before (Xiao Y. et al., 2020) and following (Huang et al., 2020; Hung et al., 2020; Ishiguro et al., 2020; Nowak et al., 2020; Vacchiano et al., 2020; Yan et al., 2020; Zhang et al., 2020b) admission and treatment. In children, Zhang C. et al. (2020) reported diarrhoea as an initial symptom in 4/34 (11.8%), and Chen J. et al. (2020) in 1/12 (8.3%) patients, of whom a total of 4 (33.3%) would develop diarrhoea.

Shang et al. (2020) recorded "three or more loose or liquid stools per day" in 157/564 patients (27.8%). Most cases passed 3 or 4 stools per day, but in some cases this exceeded 10/day; of these 157, 79 (50.3%) patients' diarrhoea was "loose", and 78 (49.7%) "watery".

Xiao Y. et al. (2020) reported diarrhoea at presentation in 90/ 912 (9.9%) cases, and characterised it in 50 instances. It was "mushy" in 14 cases (28%), "loose" in 4 cases (8.0%), and "watery" in 32 cases (64.0%); the duration was given in 63 cases, being 1–3 days in 40 (63.4%), 4–6 days in 17 (27.0%), and >6 days in 6 (9.5%) cases.

In Huang et al. (2020), 3 of 8 (37.5%) young adults presented with diarrhoea, and a further 3 (37.5%) developed diarrhoea during hospitalisation; it occurred up to 6 times per day.

Ishiguro et al. (2020) reported diarrhoea for a mean of 7 days among 6/11 (55.6%) patients, with a maximum duration of 14 days. In this case, the patient had diarrhoea for 10 days in the community before hospitalisation.

Ai et al. (2020) reported diarrhoea at presentation in 2/142 (1.4%) patients, and throughout the disease in 6/142 (4.2%), although they only counted those with GI symptoms over ≥ 3 days in the inpatient setting. They recorded diarrhoea which was mostly watery, lasting up to 14 days.

Zhang et al. (2020a) described diarrhoea in 91/409 (21.0%) severe adult cases; in this population, the mean duration was 4.4 days, at a mean frequency of 4.5 episodes/day. Diarrhoea was described as "loose" in 37 (40.7%), and "watery" in 54 (59.3%) cases.

Zhang H. et al. (2020) tracked symptoms in 505 patients, documenting diarrhoea in 62 (12.3%). They reported that:

"Patients' diarrhoea frequency was between 3 and 10 times per day. Most of them passed thin pasty yellow or watery stools [...]".

Wei et al. (2020) reported on a cohort of 84 healthcare workers, 26 (31.0%) of whom experienced diarrhoea, defined as three or more loose or liquid stools per day. It occurred up to 14 times/day, with a mean of 5.7 episodes/day before treatment, and lasted a mean 3.7 and a maximum of 14 days, with a mean of 5.7, episodes/day before treatment. The mean Bristol score was 5.9, or visual analogue scale (VAS) mean 6.8, described by the authors as "pasty".

Pan et al. (2020) reported diarrhoea in 35/204 (17.2%) patients. "Cases of diarrhoea were usually not high volume or clinically severe, but more commonly presented as nondehydrating loose stools, typically up to thrice daily", indicating the inclusion of patients passing fewer than three loose stools/day. Similarly Lin et al. (2020) recorded diarrhoea in 5/95 (5.3%) patients at onset, and 23 (24%) in total, presenting as 2–10 loose or watery stools/day.

Han C. et al. (2020) reported on a cohort of 206 adults with mild disease, 67 (32.5%) of whom had diarrhoea lasting from 1 to 14 days (mean 5.4), comprising up to 18 (mean 4.3) episodes/day. 35 (52.2%) of those patients with diarrhoea described it as "watery", as opposed to "loose". 23 did not report any respiratory symptoms, and diarrhoea did not coincide with fever in 18 patients; it preceded or coincided with the onset of respiratory symptoms and fever in 13 and 44 cases respectively.

Other Subgroups

A number of studies looked at the manifestations of Covid among those with preexisting conditions. Methods varied, with some retrospectively analyzing a wider cohort, one matched casecontrol study, and some reporting data only on their selected group. Here, the significance of variations in the rate of diarrhoea is appraised using Fisher's exact test where either group in the cohort contains fewer than 500 cases (one-tailed unless stated); otherwise, Chi-square is used. In those cases with no form of control group, comparison is made to the adult reference figure of 4506/18,180 (16.0%). Studies investigating the same or related diseases or conditions are pooled in order to increase the statistical power of analysis.

Ellington et al. (2020) reported diarrhoea in 497/3474 (14.3%) pregnant women with Covid across the United States with symptoms described on the CDC database, as opposed to 10,113/43,855 (23.1%) of their non-pregnant peers; this is a significant difference (Chi square, $p = 1 \times 10^{-32}$). (Cao et al., 2020; Chen H. et al., 2020; Liu D. et al., 2020; Wu Y.-T. et al., 2020; Yin et al., 2020; Yu et al., 2020) gathered data on pregnant women hospitalised with Covid in Wuhan, among whom 7/70 (10.0%) had diarrhoea. Of 88 pregnant women in France with Covid-19 who responded to a survey, 18 of whom were hospitalised, 28 (31.8%) reported diarrhoea (Cohen et al., 2020).

Guerra et al. (2020) and Taxonera et al. (2020) reported on cohorts of irritable bowel disease (IBD) patients in Spain with Covid. They reported diarrhoea in 35/82 (42.7%) and 9/12 (75.0%) patients respectively, giving a pooled prevalence of 44/ 94 (46.8%), although a more stringent definition of diarrhoea was adopted than elsewhere. Palaiodimos et al. (2020) investigated the impact of obesity on clinical course and prognosis in Covid in patients in the United States (NY). Patients were placed into groups of BMI <25 (healthy weight), $25 \le BMI <35$ (overweight-obese), and $35 \le BMI$ (severely obese). The prevalence of diarrhoea in these groups was 8/38 (21.1%), 35/116 (30.2%), and 23/46 (50.0%) respectively. In each pair of adjacent groups, there was a significant positive association between obesity and the incidence of diarrhoea ($p = 4 \times 10^{-5}$, p = 0.007).

Li et al. (2020) analysed the association between cardiovascular disease, and the clinical course and prognosis of Covid patients. Within their cohort, 25/566 (4.4%) of those without cardiovascular disease had diarrhoea, compared to 8/ 89 (9.0%) of those with cardiovascular disease. This is not significantly different to those seen in the broader adult population (p = 0.08) or those seen in their control group (p = 0.11-both Fisher's exact test, two-tailed).

Du H. et al. (2020) compared children with Covid with and without allergies in Wuhan, 1/43 (2.3%) and 8/139 (5.8%) of whom had diarrhoea respectively; this is not a significant difference (p = 0.688-Fisher's exact test, 2-tailed).

Mathian et al. (2020) reported diarrhoea in 7/17 (41.2%) Covid patients with lupus erythematosus across France; this is significantly higher than among the wider adult population (p = 0.0118).

Wang F. et al. (2020) reported diarrhoea in 12/28 (42.9%) diabetic Covid patients in Wuhan; this is significantly higher than among the wider adult population (p = 0.0007).

Dhakal et al. (2020) and Gonzalez-Lugo et al. (2020) reported on Covid patients with multiple myeloma and monoclonal gammopathy respectively, in the United States (Wi. and NY). Each recorded diarrhoea in 1/7 patients, giving a pooled prevalence of 2/14 (14.3%). This is not significantly different to the general adult population (p = 1.00-Fisher's exact test, 2tailed).

Wang R. et al. (2020), and Sachdeva et al. (2020) reported on renal patients with Covid. Respectively, 5/7 (71.4%) haemodialysis patients in Wuhan and 6/11 (66.7%) with endstage kidney disease in the United States (NY) experienced diarrhoea; the pooled prevalence in this group was 11/18 (61.1%), significantly higher than the wider adult population $(p = 2 \times 10^{-5})$.

Wu et al. (2020b) studied a cohort of Covid patients in Wuhan with various haematological malignancies, and Hussain et al. (2020) reported on patients with sickle-cell anemia. Rates of diarrhoea in these cohorts were 0/6 and 1/4 (25.0%) respectively, with a pooled prevalence of 1/10 (10.0%); this was not significantly different to the general adult population (p = 1.00–Fisher's exact test, 2-tailed).

Benkovic et al. (2020) and Ridgway et al. (2020) reported on US patients with HIV, reporting diarrhoea in 1/4 (25.0%) patients in NY and 3/5 (60.0%) in II. respectively, giving a pooled prevalence of 4/9 (44.4%). This is significantly higher than in the wider adult population (p = 0.042).

Several studies have addressed cohorts of solid organ transplant recipients; rates of diarrhoea were reported to be 10/ 14 (71.4%) in Italy (Cavagna et al., 2020), 16/53 (30.2%) in Sweden (Felldin et al., 2020), 4/18 (22.2%) in Spain (Fernández-Ruiz et al., 2020), 7/21 (33.3%) in Switzerland (Tschopp et al., 2020), 1/7 (14.3%) in the United Kingdom (Banerjee et al., 2020); in the United States, rates were 26/47 (55.3%) (Mi.) (Chaudhry et al., 2020) and 8/36 (22.2%) (NY) (Akalin et al., 2020). The pooled prevalence of diarrhoea was 72/196 (36.7%), significantly higher than among the general population ($p = 3 \times 10^{-12}$). Chaudhry et al. (2020) included a control group of hospitalised Covid patients without solid organ transplants, of whom 17/100 (17%) had diarrhoea; this is significantly lower than in those with transplants ($p = 4 \times 10^{-6}$).

SARS–CoV-2 in Faeces and Urine

The presence of SARS-CoV-2 RNA in stool and urine has now been widely documented, and has been reviewed elsewhere (Jones et al., 2020); nevertheless, a systematic review was undertaken in order to identify those trends most relevant in this context. Using the same parameters set out in the previous section, PubMed and Scopus were searched for (Covid OR SARS-CoV-2) AND (stool OR "faeces" OR urine). 565 papers were identified, of which 96 were exclusive to Pubmed, 190 were exclusive to Scopus, and 279 appeared on both. Titles and abstracts were reviewed to identify 88 cohort studies. Of these, 49 and 20 included data on virus in faeces and urine, and are presented in Supplementary Appendix 2, 3 respectively. Excluding studies in which the cohorts may have overlapped, 30 and 14 studies were included in a pooled analysis, in which viral RNA was detected in the stool of 328/1168 (28.1%) adults and 83/161 (51.6%) children, and in the urine of 9/233 (3.9%) adults and 2/31 (6.5%) children.

Concentration

Reported values of viral RNA in stool reached a maximum of $O(10^{10})$ copies/ml, although values of 10^6-10^8 were much more widespread. Lui et al. (2020) reported maximum and median concentrations of 10^{6.4} and 10^{4.1}/ml. Hung et al. (2020) took stool samples at the beginning of their study, reporting concentrations as high as 10¹⁰ copies/ml, although typical concentrations appeared to be around $10^{3.3}$. Wang W. et al. (2020) reported cycle thresholds corresponding to median, 95th percentile, and maximum concentrations of $10^{4.0}$, $10^{4.6}$, and $10^{6.8}$ /ml. Of 20 patients with viral RNA detected in the faeces, Wang X. et al. (2020) presented data on the concentration from those 11 patients whose stool remained positive after respiratory swabs. Of these, several produced samples with cycle thresholds of 25-27, corresponding to a viral RNA load of 10^{5.5}-10^{6.0}/ml. Wölfel et al. (2020) reported that faecal viral RNA reached 10^7 copies/ml in 3 of 8 positive cases.

In children, Du W. et al. (2020), reported mean faecal viral RNA loads of $10^{6.5}$ /ml, and a maximum of $10^{7.4}$. Han M. S. et al. (2020) observed the progression of concentrations, recording median and maximum concentrations in the 1st, 2nd and 3rd weeks of sampling of $10^{8.0}$ and $10^{10.3}$; $10^{7.3}$ and $10^{9.0}$, and $10^{7.6}$ and $10^{8.7}$; the values across all subsequent sampling were $10^{7.6}$ and $10^{8.6}$ /ml.

Some authors reported only cycle thresholds, rather than concentrations (Young et al., 2019; Bonetti et al., 2020; Kujawski et al., 2020; Wu et al., 2020a). Of these, Wu et al. (2020a) provided the greatest detail, showing the cycle threshold of each test conducted. The cycle threshold of different genes within the same sample often varied sharply, with no consistent pattern discernible. Where other authors have provided less detail, it is impossible to say how much unexplained variation in the experimental data this might mask. Muenchhoff et al. (2020) compared the results from a selection of Covid PCR tests, and found that the concentrations corresponding to different cycle thresholds were similar, with variations not generally greater than a factor of three. However, this work also demonstrated that poorly designed tests can produce inconsistent and misleading results. The relationship between cycle threshold and copy number also depends on the dilution of the sample, which is not described in detail by all authors.

Jeong et al. (2020) found viral RNA in the urine of 5/5 adults tested, at concentrations between $10^{0.59}$ and $10^{2.09}$ /ml. Peng et al. (2020) reported $10^{2.5}$ /ml in the urine of 1/9 (11.1%) patients tested. Kim et al. (2020) reported viral RNA in the urine of 2/54 (3.7%) patients in a mixed cohort, having an average of $10^{4.9}$ /ml.

Han M. S. et al. (2020) reported $10^{7.55}$ and $10^{3.82}$ copies/ml in the urine of two mildly symptomatic infants.

Duration

Viral RNA in stools was widely reported to outlast that detected in respiratory swabs (**Supplementary Appendix 2**). It is difficult to determine an average duration due to the infrequency of sampling and high numbers of patients who were still shedding virus at the end of their studies, however authors suggested values of 22.3 days (He et al., 2020), 19.3 days (Lo et al., 2020) and 22 days (Zheng et al., 2020), and 28.9 days in children, decreasing with age (Chen Z. et al., 2020). In extreme cases, virus continued to be shed up to 103 (He et al., 2020) and 49 days (Wu et al., 2020a) from onset in adults, and for up to 65 days (Liu P. et al., 2020) in children. Liu P. et al. (2020) found that viral RNA in stool outlasted that in respiratory samples by a median of 25 days among children.

Most patients whose stool samples contained viral RNA contained it from the commencement of sampling, although there were some exceptions. Wu et al. (2020a) reported that in a cohort of 74 patients, 12 (16.2%) had detectable faecal viral RNA only after respiratory swabs had turned negative, with a delay of up to 17 days; the same observation was made of 1 of 11 (9.1%) patients by Lui et al. (2020), and in 2 of 69 (2.9%) patients in Wang X. et al. (2020). There have been instances in which RNA becomes undetectable in stool samples before reappearing (Du W. et al., 2020; Lo et al., 2020). Viral RNA was detected in the stool of 6/18 (33%) asymptomatic children by Xiong et al. (2020), and three of three asymptomatic children by Han M. S. et al. (2020).

The pattern of small numbers of patients shedding virus for an extended period was also observed in SARS-CoV-1 (Leung et al., 2003; Peiris et al., 2003). As with assessments of the prevalence of diarrhoea, the programme of sampling significantly influenced the reported figures. Where investigators tested only once or twice in adult or mixed cohorts, SARS-CoV-2 RNA was reported in the faeces of 30/260 (11.5%) of patients. Where more intensive programmes of sampling were undertaken, RNA was detected in the faeces of 205/397 (57.8%) patients.

Association Between Diarrhoea and the Presence of SARS-CoV-2 in Faeces

Association between diarrhoea and the presence of viral RNA in stool has widely been taken as an indicator of active infection of the digestive tract, which would seem to increase the likelihood of viable virus in stools. Furthermore, the continued viability and aerosolisation of any virus may vary with the consistency of the stool, and so the concentrations anticipated in building drainage systems must be determined with reference to the characterisation of stool, and the virus within it.

Wei et al. (2020) reported that 18/26 (69.2%) and 10/58 (17.2%) of those with and without diarrhoea produced positive stool swabs respectively ($p = 8 \times 10^{-6}$ -Fisher's exact test), and that stool swabs were significantly more likely to remain positive for longer than pharyngeal swabs among patients with diarrhoea (6/26 (23.1%), 2/58 (3.4%); p = 0.01). A further two papers presented data on prevalence in patients with and without diarrhoea: Chen Y. et al. (2020) reported the detection of viral RNA in the stool of 6/7 (85.7%) patients with diarrhoea and 22/35 (62.6%) of those without (p = 0.39), and Wang X. et al. (2020) reported the detection of viral RNA in 5/12 (41.6%) of those with diarrhoea and 15/57 (28.3%) of those without (p = 0.31).

Bonetti et al. (2020) noted an association between diarrhoea and the concentration of viral RNA in positive samples, although the observed positive association was not statistically significant (p = 0.056). Similarly, Yin et al. (2020) reported that the mean cycle threshold of positive samples from patients with diarrhoea was 31.37, as compared to 36.09 from those without.

Virus has been detected directly in diarrhoea (Holshue et al., 2020), and in firm stool (Park et al., 2020; Wang W. et al., 2020).

Presence of Viable Virus in Faeces or Urine

In reviewing the presence of viable virus in samples, important evidence was found outwith the papers presented in the systematic review; this is a rapidly advancing field.

Chen X. et al. (2020) presented the case of a seven-year-old girl with diarrhoea alongside "classical" Covid symptoms, with "abundant" viable virus in her faeces, although no further details on this were given.

Wei et al. (2020) and Xiao et al. (2020b) report the existence of data not published in full elsewhere in the literature, showing the isolation of SARS-CoV-2 from stool. Wei et al. (2020) state that viable virus was found in the faeces of 19 patients. Xiao et al. (2020a) subsequently published a report showing the successful culture of SARS-CoV-2, from the stool of two of three patients selected for the presence of viral RNA by PCR, on Vero E6 cells. One of these patients was studied in more detail, and later stool samples did not yield culturable virus, even as viral RNA remained detectable.

Wang W. et al. (2020) tested stool samples from four patients, of which samples from two patients without diarrhoea were said to contain viable virus.

Kim et al. (2020) used a CaCo-2 cell line (ultimately of human colorectal epithelial origin) to attempt to culture SARS-CoV-2 from 13 stool and two urine, as well as nine serum samples, containing viral RNA. Virus could not be isolated from any of these samples.

Jeong et al. (2020) attempted virus isolation from faecal suspension and urine on ATCC CCL-81 cells, however the samples were found to be cytopathic. 2/2 patient urine samples (10^{1.51} and 10^{2.09}/ml), and 1/1 patient faecal supernatant (faecal RNA concentration 10^{2.18}/ml, diluted by a factor of 10; all inocula 500 µl) appeared to induce "moderate increases in body temperature, rhinorrhoea and decreased activity at 4 dpi [days post-infection] which persisted until 6 dpi" in intranasally inoculated ferrets. Viral loads were detected in ferret nasal wash between $10^{0.35}$ – $10^{3.24}$ /ml, with isolation on Vero cells successful only on those samples at $\geq 10^{1.68}$ /ml. The observed symptoms and viral loads in ferrets are consistent with previous work by the same team, which did include a negative control (Kim et al., 2020), however contrast with the asymptomatic infection of ferrets reported by Kutter et al. (2020) and Schlottau et al. (2020). The viral loads in patient samples here are much lower than those reported elsewhere, and those in ferrets are much lower than in Schlottau et al. (2020) and Shi et al. (2020).

SARS-CoV-2 in Aerosol

There has been much controversy over the labeling of Covid-19 as an airborne disease, although this is now generally accepted as an important mode of transmission. In many contexts the term "airborne" is suggestive of virions becoming aerosolised in the human respiratory tract, and remaining suspended and viable for many hours. This has been at the crux of much of the wider debate on the adoption of the term "airborne", but has little bearing on the spread of SARS-CoV-2 through the building drainage system, and its designation as such in this context (Wilson et al., 2020; editorials in: CDC, 2020; Nature, 2020; WHO, 2020).

Liu Y. et al. (2020) measured viral RNA in droplets and aerosol in air sampled from two hospitals dedicated to the treatment of Covid patients. Viral RNA was detected in particles in all size ranges investigated, from <0.25 to >2.5 μ m. The highest concentrations in patient areas were found in a WC, although the detection method employed here did not differentiate between particle sizes. This was an unventilated space, implying a local source for the droplets and aerosol detected, rather than transfer on building air flows. However, the lack of ventilation precludes comparison between the rate of particle generation here and in ventilated spaces.

van Doremalen et al. (2020) report that the half-life of viable SARS-CoV-2 in aerosolised tissue culture medium (Dulbecco's modified Eagle's medium; DMEM) is very similar to that of SARS-CoV-1. Particles of $<5\,\mu$ m were generated in a 3-jet Collison nebuliser and suspended in a Goldberg drum, wherein the half-life of SARS-CoV-1 was 1.18 h and that of SARS-CoV-2 was 1.09 h at 65% relative humidity (RH) and 21–23°C. However, under these experimental conditions, viable aerosolised SARS-CoV-2 was found at only one tenth the concentration of viable aerosolised SARS-CoV-1.

Smither et al. (2020) compared the aerosolisation and subsequent survival of SARS-CoV-2 (England-2 strain) in DMEM and simulated saliva. Aerosols of $1-3\,\mu m$ were generated in a 3-jet Collison nebuliser and suspended in a

TABLE 1 Half-life of aerosolised SARS-CoV-2 under different conditions-data
from Smither et al., 2020.

0.7
2.8

dark Goldberg drum at RH 40–60% or 68–88%, at 19–22°C. The culture assay showed that the artificial saliva produced a density of viable aerosolised virus around ten times less than that of the DMEM [TCID₅₀ of O (10^1) as opposed to O (10^2)/L], which was attributed to a lower particle generation rate rather than virus inactivation. The half-life of the virus in different media and at different humidities is presented in **Table 1**. Increased humidity was associated with diminished recovery of viable virus in aerosol in DMEM, but with increased recovery in simulated saliva.

Pathogen Aerosolisation (Theory)

The concentration of suspended matter in aerosol can be characterised by an Enrichment Factor (EF); where applied to the recovery of viable microorganisms, this has often been found to be greater than unity (Blanchard and Syzdek, 1970; Blanchard and Syzdek, 1972). Many microbes and viruses exhibit surfaceactive effects. This leads to the accumulation of waterborne microbes at the liquid interface, including that at the surface of bubbles passing through the liquid and adjacent to suspended solids. The EF of bacteria has been observed to vary between droplets within a population, depending on their mode of formation; between different organisms, and between different strains of the same organism; and with the presence of other impurities in the water; interaction effects have also been noted between these factors (Blanchard, 1978; Blanchard and Syzdek, 1978; Baron and Willeke, 1986). Further influences include the generation fluid, the temperature, and the humidity, and radiation (Kim et al., 2007). Whereas much of this research has been conducted with aerosol generated by bubbles, other relevant modes of droplet production include spraying, and droplet breakup and impaction (Xu and Weisel, 2005). The partition of microbes and other contaminants by these modes has not been well described, and the contribution of each mode within the building drainage system is not known.

Many researchers have identified interacting factors which influence the tendency of viruses to flocculate or coagulate, including the nature of other solids present in suspension, the ionic strength and pH of the suspension, and the size of the virion (Xagoraraki et al., 2020). Additionally, increasing hydrophobicity-associated with lipid shells-increases the tendency of viruses to adsorb to solid substrates (Kinoshita et al., 1993). These effects are likely to play a role in the formation of bioaerosols, and their subsequent transport and ongoing viability, however this remains poorly characterized (Lin and Marr, 2017). SARS-CoV-2 virions are spherical, of 70–90 nm diameter (Kumar et al., 2020).

Pathogen Aerosolisation (Observed)

The role of the building drainage wastewater system as a pathway for disease transmission is supported by a body of evidence for the creation and diffusion of bioaerosols at and from sanitary fittings. WCs have attracted particular attention.

Gerba et al. (1975) studied the isolation of MS2 (c. 27 nm dia., unenveloped), poliovirus [c. 30 nm; unenveloped (Romero and Modlin, 2015)], and *Escherichia coli* [rods; $1.1-1.5 \times 2.0-6.0 \mu$ m, often paired; often with flagella, multifarious fimbriae especially common in pathogenic strains (Scheutz and Strockbine, 2015)], from flushing WCs. All of these were recovered from gauze covering the WC bowl, and from exposed plates on bathroom surfaces. The form of the inoculum—culture, homogenised stool, or stool "pellet"—was found to exert little influence on the recovery of bacteria. This finding replicated that of Newsom (1972), working with a range of bacteria.

Barker and Jones (2005) used a single-stage impactor to detect viable MS2 and Serratia marcescens [rods; $0.5-0.8 \times 0.9-2.0 \mu m$; usually with flagella (Grimont and Grimont, 2015a)] in the air following a toilet flush; both were selected partially for their good environmental stability. c. 10¹⁰ MS2 virions or cells in a semisolid agar were seeded onto the exposed surfaces of a WC. Following flushing of the WC, viable MS2 was recovered from the air at 2420 PFU/m³ after 1 min, 178 PFU/m³ after 30 min, and 27 PFU/ m³ after 60 min, and culturable bacteria at around half that concentration. The reduction in the airborne bacteria with subsequent flushes was between 2.4 and 3.9 times, while bacteria retrieved from the toilet surfaces and water diminished by around two orders of magnitude per flush. This could be attributable to and illustrative of the enrichment of aerosol, although effects relating to the adsorption and elution of bacteria are also possible. Single-stage impactors are typically inefficient below around 4 µm, although this is less problematic when working with bacteria than with viruses. They were also used to demonstrate the diffusion by toilets of Salmonella enteritidis [rods; $0.7-1.5 \times 2.0-5.0 \,\mu$ m; with flagella (Popoff and le Minor, 2015)] from a relatively inviscid inoculum (Barker and Bloomfield, 2000), and Clostridium difficile [rods; $0.5-1.9 \times 3.0-16.9 \,\mu$ m, sometimes chained; typically with flagella (Rainey et al., 2015)] from faecal suspension (Best et al., 2012), the latter up to 90 min post-flush.

Moore et al. (2015) demonstrated the recovery of aerosolised MS2 from above a home spa. Given a concentration of 27,000 PFU/cm³ in the pool water, 528 PFU/m³ were present 10 cm above the pool edge; mean concentrations taken at sampling points \geq 25 cm hence horizontally and/or 90 cm vertically, were no more than 11 PFU/m³.

Gormley et al. (2017) modelled the spread of a pathogen through a building drainage system using *Pseudomonas putida* [typically rods; typically c. 5 μ m long; >1 flagellum (Palleroni, 2015)]. The inoculum was disseminated by a simulated toilet flush into the ground floor level of a two-storey test rig constructed in accordance with (BS EN 12056-2, 2000), and air flow was induced by a typical extract fan from a chamber at the level of the first floor. Viable organism was retrieved from the air in the test chamber using a single stage impactor, and cultured from the interior surfaces of the dry WC.

Newsom (1972) compared the aerosolisation by flushing toilets of several strains of bacteria; the numbers of CFUs per unit air sampled were highest for Achromobacter [rods $0.8-1.2 \times$ 2.5-3.0 µm; 1-20 flagella (Busse and Auling, 2015)] and Pseudomonas spp. [rods, $0.5-1.0 \times 1.5-5.0 \mu m$; fimbriae more common in pathogenic strains; typically ≥ 1 flagellum (Palleroni, 2015)], intermediate for Enterobacter cloacae [rods; $0.6-1.0 \times$ 1.2-3.0 µm; fimbriae more common in pathogenic strains; 4-6 flagella (Grimont and Grimont, 2015b)], Proteus spp. [rods, $0.4-0.8 \times 1.0-3.0 \,\mu\text{m}$; fimbriae common, sometimes involved in pathogenesis; typically ≥ 1 flagellum (Penner, 2015)], and Shigella sonnei [rods; $1-3 \times 0.7-1.0 \,\mu\text{m}$; nonmotile (Strockbine and Maurelli, 2015)], and lowest for E. coli, Klebsiella pneumoniae [rods; $0.3-1.0 \times 0.6-6.0 \,\mu\text{m}$; often paired or in short chains; hydrophilic capsule, sometimes with fimbriae, nonmotile (Grimont and Grimont, 2015c)], Salmonella typhimurium (as S. enteritidis), and Serratia spp. (as S. marcescens).

Lai et al. (2018) reported much higher EFs from a toilet flush for *Staphylococcus epidermis* (spherical, 0.96 μ m, nonmotile) than for *Escherichia coli* and *Pseudomonas alcaligenes*; the authors suggested that the latters' larger size may have been responsible for this. Their experiments with each bacterium encompassed a range of initial concentrations, and demonstrated an inverse association between initial concentration and EF in nine of ten datasets presented.

Work with viruses has been more limited. The influence of surface-active effects was demonstrated by Morrow (1969), who showed that the accumulation of foot-and-mouth-disease virus (c. 25 nm, non-enveloped) at the air-water interface could be driven by bubble generation. Baylor et al. (1977) showed the aerosolisation of TS2 and TS4 bacteriophages (both proteinsheathed) on jet droplets, with EF around 50. In Gerba et al. (1975), the bioaerosols generated by toilet flushing contained more culturable units of poliovirus than E. coli under the same conditions, even though the number of E. coli seeded into the toilet was greater. Fischer et al. (2016) found that different strains of Zaire ebolavirus formed viable bioaerosols at differing rates. Kim et al. (2007) found that the recovery of Transmissible Gastroenteritis Virus, an α-coronavirus around 100 nm diameter (Salanueva et al., 1999; Escors et al., 2001) was minimally sensitive to nebuliser design and pressure, suggesting that physical stresses do not significantly degrade viruses during the aerosolisation process in this context. The recovery of viable bioaerosols decreased with increasing relative humidity.

Lin and Marr (2017) showed modest levels of viable bioaerosol generation at converging near-horizontal pipes using bacteriophages MS2 and Phi6 (c. 75 nm dia.; lipid envelope) in digested sewage sludge. The rate of isolation of Phi6 from the air was two orders of magnitude less than that of MS2 in both tests conducted, given the same concentration in the bulk liquid. When tested in a Collison nebuliser, the number of bioaerosols generated varied only by a factor of two.

Aerosol Generation and Size Distributions

In Lin and Marr (2017), the peak aerosol concentrations were in the region $0.03-0.3 \mu m$, across converging near-horizontal pipes, a model aeration basin, and toilet plume. Similarly, Lai et al.

(2018), investigating four different toilet flushes, reported that in all cases most particles were of diameter less than 0.6 μm , given a minimum size for detection of 0.3 $\mu m.$

Baron and Willeke (1986) measured the particles above the surface of a spa whirlpool under different operating conditions, in the range $0.7-16 \,\mu\text{m}$. The particle concentration increased sharply toward the lower limit of detection, at $0.7 \,\mu\text{m}$ whether the pool was on or off, and at a range of water temperatures. No particles above 9 μm were detected, and in all cases at least 90% of particles were of diameter <4 μm . This finding was replicated by Moore et al. (2015).

Xu and Weisel, (2005) used an optical particle sampler sensitive down to 0.1 µm to measure the aerosols present during a hot shower, at breathing height. Particles between 0.1 and 0.3 µm initially comprised around 60% of those detected, rising to and stabilising at around 75% from the second minute of the 10-min shower. Zhou et al. (2007) also investigated particles in the in-shower breathing zone, using an erodynamic particle sampler stated to have been effective for erodynamic diameters of 1-30 µm. Their shower contained a mannequin, and was tested with hot and cool water, and with three different shower heads associated with different flow rates. The emphasis of this study was on mass fraction, and no particles below 1.8 µm were reported using warm water. The use of cold water reduced the total mass of particles recovered, however a much greater proportion was associated with smaller aerosol, which were reported down to diameters of 0.5 µm; median particle diameters were around 1 µm diameter, with 90% of particles below 2 µm. In all cases, more particles were generated at higher flow rates. As in Xu and Weisel (2005), the distribution of particle sizes varied little during a 10 min experiment.

Gormley et al. (2020b) produced the only known result in the literature documenting the size of airborne particles within a model building drainage system, down to a lower limit of detection of 0.5 μ m. In all presented datasets, the peak concentration occurred below 1 μ m, with a dropoff at the lower end of this scale. They were able to demonstrate the transit of viable *Pseudomonas putida* the equivalent of one storey, taking from 48 to 155 s under the same configuration as in Gormley et al. (2017).

It must be noted that in the foregoing, populations of particles below the limits of detection could play an important role in the transmission of virions of the order of 10 nm, if present in sufficient concentrations.

Gormley et al. (2014) demonstrated the transit of a smoke particle tracer through the drainage system of a house under naturally occurring conditions, with a simulated trap failure. Hung et al. (2006) showed that sulphur hexafluoride tracer gas was drawn up through the building drainage system of a building similar to Amoy Gardens by a domestic extract fan, rising eleven storeys in 3 min. They further demonstrated that the tracer was entrained by water flowing down the stack, and could be driven through a depleted trap near the base of the stack where an offset in the pipework contributed to positive pressure generation.

Conditions in Building Drainage Systems

Gormley et al. (2013) investigated the conditions in a hospital drainage stack in Scotland and found temperatures of around 24°C, with relative humidity at or very near to 100%. Transitory air flows in both directions were observed at the top of the stack, with upwards flow in one stack perhaps driven by air entrainment in an adjacent stack, this suggesting another, unsteady-state mechanism by which aerosol might be driven upwards through drainage systems. Conditions in the stack were broadly constant over the course of 1 week, and a literature review identified studies of conditions in sewers, which suggested little variation globally. However, this review identified a lack of data on conditions within the BDS, where many factors might influence the conditions between and even within different buildings. For example, in contrast with the stack examined here, that at Amoy Gardens was external to the building, and under the generally accepted failure conditions, would have been drawing large volumes of air in from indoors (Jack et al., 2006).

Mitigation–Regulation and Practice

American, European and British regulation have historically been written to avoid the loss of trap seals due to siphonage or blowout (Swaffield et al., 2005a); evaporation is often afforded less attention (CIBSE, 2014: Guide G; BS EN 12056-2, 2000), or ignored (Department of Health (UK), 2013). Evaporation is not mentioned in the main text of BS:EN 12056, however the National Annex cites the risk of evaporation specifically from floor gullies, suggesting that they should only be sited where they would be adequately replenished. These documents also seem to understate the risk attendant on trap failure, referring not to the spread of pathogens but to "odours", "vapours", and "foul air", framing the integrity of traps as a matter of comfort rather than life safety. The Health Building Note HBN 00-09: Infection Control in the Built Environment (Department of Health (UK), 2013), addressing the spread of pathogens via other building services, cites risks from bacteria and protists in the water supply; no mention whatsoever is made of viruses.

Given the state of the knowledge on the spread of pathogens *via* the BDS, there are several simple, established technologies which seem likely to effectively mitigate this risk, particularly with the development of a more amenable regulatory environment.

Early BDS were generally "two-pipe" systems, with separate stacks and ventilation for the disposal of blackwater (that containing human excreta), and greywater (e.g. from sinks and baths) (Swaffield et al., 2005b). One-pipe systems were generally adopted from the mid-20th century for reasons of economy, but two-pipe systems are acknowledged as an acceptable configuration in BS:EN 12056, and remain in use in many older buildings. Twopipe systems are however proscribed in some jurisdictions.

Hung et al. (2006) noted the widespread practice of using one trap to service multiple appliances in Hong Kong; this arrangement can conveniently be retrofitted where regulations permit, as was seen in the aftermath of the Amoy Gardens outbreak. Typically, all the greywater fittings within a bathroom are connected to the same trap, which consequently is replenished by the use of any of the appliances. Lowevaporation floor drain traps have also been developed, which retain the intended functionality of conventional floor drain traps given infrequent use (Chan et al., 2008).

There are also now waterless traps, typically consisting of a silicone sheath which opens under the weight of wastewater, or in response to negative air pressure in the drainage system (Swaffield et al., 2005a); these have found extensive use in practice (Gormley and Beattie, 2010; Gormley et al., 2017). However, their function is not regulated by any standard, which may decrease confidence in their adoption; they are also vulnerable to blockage by solid matter (CIBSE, 2014). The main text of BS:EN 12056 specifies that appliances must be fitted with a "trap", defined as a "device that prevents the passage of foul air by means of a water seal"; however, the National Annex suggests their use particularly in floor gullies in closely controlled environments where their condition can be adequately monitored. This raises a legitimate concern about their use in domestic environments. Furthermore, it is not clear whether this permits common trapping as described in Hung et al. (2006); this is generally avoided in practice in Europe.

CIBSE (2014) suggests the use of self-replenishing traps for condensate drains, which are liable to dry out over long periods of inactivity. BS EN 12056-2 (2000) provides for the use of stub stacks, which can help to avoid trap blowout due to large pressures in the drainage stacks of tall buildings.

The risk of trap blowout due to transient pressure waves caused by the sudden interruption of air flows, such as by backup, water curtain formation, or branch discharge into the stack, can be mitigated by attenuating the pressure waves. (Swaffield et al., 2005a, Swaffield et al., 2005b) developed a positive air pressure transient attenuator (PAPA) for this purpose, the use of which has been demonstrated experimentally and in the field. Kelly et al. (2008) demonstrated the use of pressure waves as relatively lowamplitude vibrations to identify vacant trap seals on a BDS.

CONCLUSION

Although the prevalence of diarrhoea in SARS-CoV-2 is less than that in SARS-CoV-1, there are nevertheless a large number of patients in the community who develop gastrointestinal symptoms, some of whom may never be recognised as having Covid-19. Viral RNA in stool may persist for weeks or months, however it is most abundant around the second week of illness. Concentrations are probably similar to those found in SARS-CoV-1, although the difficulties of quantification mean that comparisons to historical data must be drawn with caution. Culturable virus was less persistent. Many groups of patients with pre-existing conditions were more likely to develop diarrhoea with Covid 19, however no evidence could be found comparing the prevalence and concentration of virus detectable by PCR or culturable from faecal matter. Although diarrhoea has generally been cited as a causative factor in the SARS-CoV-1 outbreak at Amoy Gardens, several investigators have shown that the aerosolisation of viable bacteria in toilet plumes occurs at similar rates from solid stool; there is no comparable evidence from within the BDS.

Limited data suggest that SARS-CoV-2 aerosolises less readily than SARS-CoV-1 in a Collison nebuliser, and the ongoing viability of those aerosols remains poorly characterised. Existing evidence has been gathered in a controlled laboratory setting, and while building drainage systems are persistently warm, damp and dark, other factors such as the gases, solutes, fluids and suspended solids present may also play a decisive role in bioaerosol formation and inactivation; it must also be noted that existing evidence has been gathered over the course of hours, whereas bioaerosols can transit the BDS in a matter of minutes.

Although existing evidence of virus transmission through the building drainage system pertains mostly to particles of above 5 μ m, this appears to be due to limitations in the experimental methods employed. The generation of finer aerosol from sanitary and wastewater has been demonstrated from appliances and in "ex-building" wastewater transport and treatment. Independently, viable SARS-CoV-2 bioaerosols (\leq 5 μ m) have been demonstrated, including from aqueous suspension in a nebuliser, and viral RNA has been detected on aerosol in the submicrometre range.

The available evidence would support the possibility of SARS-CoV-2 transmission through building drainage systems, however significant gaps in the research remain. The generation of viral bioaerosols has been demonstrated from many water appliances, and in a model sewer, by a range of mechanisms. Similarly, the generation and transport of bacterial bioaerosols has been demonstrated in a model building drainage system. No attempt has been found to generate viral bioaerosols in this context, but the available evidence from related studies suggests that this is likely to be possible. There are however important factors which are inadequately addressed by the existing literature. Notably, the enrichment factor of bioaerosols has been shown to be influenced by the choice of organism, the mode of droplet creation, and the presence of impurities in the water. In addition, much of the existing research has relied on sampling techniques which omit or underreport fine bioaerosols, particularly in the submicron range. The

REFERENCES

- Abraham, P., Aggarwal, N., Babu, G. R., Barani, S., Bhargava, B., Bhatnagar, T., et al. (2020). Laboratory Surveillance for SARS-CoV-2 in India: Performance of Testing & Descriptive Epidemiology of Detected Covid-19, January 22—April 30, 2020. *Indian J. Med. Res.* 151 (5), 424–437. doi:10.4103/ijmr.IJMR_1896_20
- Ai, J.-W., Zi, H., Wang, Y., Huang, Q., Wang, N., Li, L.-Y., et al. (2020). Clinical Characteristics of COVID-19 Patients with Gastrointestinal Symptoms: an Analysis of Seven Patients in China. *Front. Med.* 7, 308. doi:10.3389/fmed.2020.00308
- Akalin, E., Azzi, Y., Bartash, R., Seethamraju, H., Parides, M., Hemmige, V., et al. (2020). Covid-19 and Kidney Transplantation. N. Engl. J. Med. 382 (25), 2475–2477. doi:10.1056/NEJMc2011117
- Banerjee, D., Popoola, J., Shah, S., Ster, I. C., Quan, V., and Phanish, M. (2020). COVID-19 Infection in Kidney Transplant Recipients. *Kidney Int.* 97 (6), 1076–1082. doi:10.1016/j.kint.2020.03.018
- Barker, J., and Bloomfield, S. F. (2000). Survival of Salmonella in Bathrooms and Toilets in Domestic Homes Following Salmonellosis. J. Appl. Microbiol. 89 (1), 137–144. doi:10.1046/j.1365-2672.2000.01091.x

role of diarrhoea in virus aerosolisation and disease transmission also merits closer attention.

There is now at least one outbreak of Covid 19 which, like the Amoy Gardens outbreak of SARS-CoV-1, can only plausibly be explained by transmission *via* the building drainage system. There exist a range of inexpensive mitigation measures which are suitable for new-build projects and retrofitting, however their adoption is often overlooked, or even impeded, due to regulation which is contradictory, outdated and varies even within nations.

Without developing a better understanding of the underlying processes, it is impossible to say how widespread this mode of transmission might be, from Covid 19, from other viruses, and from other classes of pathogen, and what measures might best mitigate the risks from each of these. What is clear in the residential sphere at least, is that designers must take a thoughtful approach which recognises the unpredictable behaviour of building occupants, and that the regulatory environment must both facilitate and require this.

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All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

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SUPPLEMENTARY MATERIAL

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- Barker, J., and Jones, M. V. (2005). The Potential Spread of Infection Caused by Aerosol Contamination of Surfaces after Flushing a Domestic Toilet. J. Appl. Microbiol. 99 (2), 339–347. doi:10.1111/j.1365-2672.2005.02610.x
- Baron, P. A., and Willeke, K. (1986). Respirable Droplets from Whirlpools: Measurements of Size Distribution and Estimation of Disease Potential. *Env. Res.* 39 (1), 8–18. doi:10.1016/s0013-9351(86)80003-2
- Baylor, E., Peters, V., and Baylor, M. (1977). Water-to-air Transfer of Virus. Science 197 (4305), 763–764. doi:10.1126/science.329413
- Benkovic, S., Kim, M., and Sin, E. (2020). Four Cases: Human Immunodeficiency Virus and Novel Coronavirus 2019 Co-infection in Patients from Long Island, New York. J. Med. Virol. 92 (11), 2338–2340. doi:10.1002/jmv.26029
- Best, E. L., Sandoe, J. A. T., and Wilcox, M. H. (2012). Potential for Aerosolisation of *Clostridium difficile* after Flushing Toilets: the Role of Toilet Lids in Reducing Environmental Contamination Risk. *J. Hosp. Infect.* 80 (1), 1–5. doi:10.1016/j. jhin.2011.08.010
- Blanchard, D. C. (1978). Jet Drop Enrichment of Bacteria, Virus, and Dissolved Organic Material. *Pageoph* 116 (2), 302–308. doi:10.1007/ BF01636887

- Blanchard, D. C., and Syzdek, L. D. (1972). Concentration of Bacteria in Jet Drops from Bursting Bubbles. J. Geophys. Res. 77 (27), 5087–5099. doi:10.1029/ jc077i027p05087
- Blanchard, D. C., and Syzdek, L. D. (1978). Seven Problems in Bubble and Jet Drop Researches 1. *Limnol. Oceanogr.* 23 (3), 389–400. doi:10.4319/lo.1978.23.3.0389
- Blanchard, D. C., and Syzdek, L. (1970). Mechanism for the Water-To-Air Transfer and Concentration of Bacteria. *Science* 170 (3958), 626–628. doi:10.1126/ science.170.3958.626
- Bonetti, G., Manelli, F., Bettinardi, A., Borrelli, G., Fiordalisi, G., Marino, A., et al. (2020). Urinalysis Parameters for Predicting Severity in Coronavirus Disease 2019 (COVID-19). *Clin. Chem. Lab. Med.* 58 (9), e163–e165. doi:10.1515/cclm-2020-0576
- Booth, C. M., Matukas, L. M., Tomlinson, G. A., Rachlis, A. R., Rose, D. B., Dwosh, H. A., et al. (2003). Clinical Features and Short-Term Outcomes of 144 Patients with SARS in the Greater Toronto Area. *JAMA* 289 (21), 2801–2809. doi:10. 1001/jama.289.21.joc30885
- Breathnach, A. S., Cubbon, M. D., Karunaharan, R. N., Pope, C. F., and Planche, T. D. (2012). Multidrug-resistant *Pseudomonas aeruginosa* Outbreaks in Two Hospitals: Association with Contaminated Hospital Waste-Water Systems. *J. Hosp. Infect.* 82 (1), 19–24. doi:10.1016/j.jhin.2012.06.007
- BS EN 12056-2 (2000). Gravity Drainage Systems inside Buildings. Sanitary Pipework, Layout and Calculation. London, UK: BSI.
- Busse, H.-J., and Auling, G. (2015). "Achromobacter," in *Bergey's Manual of Systematics in Archaea and Bacteria*. Editors M. E. Trujillo, P. Dedysh, B. DeVos, B. Hedlund, P. Kampfer, F. A. Rainey, et al. (Hoboken, NJ: John Wiley & Sons, Inc.). doi:10.1002/9781118960608.gbm00926
- Cao, D., Yin, H., Chen, J., Tang, F., Peng, M., Li, R., et al. (2020). Clinical Analysis of Ten Pregnant Women with COVID-19 in Wuhan, China: A Retrospective Study. Int. J. Infect. Dis. 95, 294–300. doi:10.1016/j.ijid.2020.04.047
- Cavagna, L., Seminari, E., Zanframundo, G., Gregorini, M., Di Matteo, A., Rampino, T., et al. (2020). Calcineurin Inhibitor-Based Immunosuppression and COVID-19: Results from a Multidisciplinary Cohort of Patients in Northern Italy. *Microorganisms* 8 (7), 977. doi:10.3390/ microorganisms8070977
- CDC (2020). Scientific Brief: SARS-CoV-2 and Potential Airborne Transmission. Available at: www.cdc.gov/coronavirus/2019-ncov/more/scientific-brief-sarscov-2.html (Accessed November 30, 2020).
- Chan, D. W., Liu, T. C., and Wong, E. S. (2008). Development of Smart Floor Traps for Enhanced Seal Protection. Hong Kong: CIB W062 International Conference on Water Supply and Drainage for Buildings.
- Chaudhry, Z. S., Williams, J. D., Vahia, A., Fadel, R., Parraga Acosta, T., Prashar, R., et al. (2020). Clinical Characteristics and Outcomes of COVID-19 in Solid Organ Transplant Recipients: A Cohort Study. *Am. J. Transpl.* 20 (11), 3051–3060. doi:10.1111/ajt.16188
- Chavarria-Miró, G., Anfruns-Estrada, E., Guix, S., Paraira, M., Galofré, B., Sánchez, G., et al. (2020). Sentinel Surveillance of SARS-CoV-2 in Wastewater Anticipates the Occurrence of COVID-19 Cases. *medRxiv*. doi:10.1101/2020. 06.13.20129627
- Chen, H., Guo, J., Wang, C., Luo, F., Yu, X., Zhang, W., et al. (2020). Clinical Characteristics and Intrauterine Vertical Transmission Potential of COVID-19 Infection in Nine Pregnant Women: A Retrospective Review of Medical Records. *Lancet* 395 (10226), 809–815. doi:10.1016/S0140-6736(20)30360-3
- Chen, J., Zhang, Z.-Z., Chen, Y.-K., Long, Q.-X., Tian, W.-G., Deng, H.-J., et al. (2020). The Clinical and Immunological Features of Pediatric COVID-19 Patients in China. *Genes Dis.* 7 (4), 535–541. doi:10.1016/j.gendis.2020. 03.008
- Chen, X., Zou, X. J., and Xu, Z. (2020). Serial Computed Tomographic Findings and Specific Clinical Features of Pediatric COVID-19 Pneumonia: A Case Report. World J. Clin. Cases 8 (11), 2345–2349. doi:10.12998/wjcc.v8.i11.2345
- Chen, Y., Chen, L., Deng, Q., Zhang, G., Wu, K., Ni, L., et al. (2020). The Presence of SARS-CoV-2 RNA in the Faeces of COVID-19 Patients. J. Med. Virol. 92 (7), 833–840. doi:10.1002/jmv.25825
- Chen, Z., Tong, L., Zhou, Y., Hua, C., Wang, W., Fu, J., et al. (2020). Childhood COVID-19: A Multicentre Retrospective Study. *Clin. Microbiol. Infect.* 26 (9), 1260.e1–1260.e4. doi:10.1016/j.cmi.2020.06.015
- Choi, K. W., Chau, T. N., Tsang, O., Tso, E., Chiu, M. C., Tong, W. L., et al. the Princess Margaret Hospital SARS Study Group (2003). Outcomes and Prognostic Factors in 267 Patients with Severe Acute Respiratory Syndrome

in Hong Kong. Ann. Intern. Med. 139 (9), 715–723. doi:10.7326/0003-4819-139-9-200311040-00005

- CIBSE (2014). *Guide G: Public Health and Plumbing Engineering*. 3rd edn. London: CIBSE.
- Clemency, B. M., Varughese, R., Scheafer, D. K., Ludwig, B., Welch, J. V., McCormack, R. F., et al. (2020). Symptom Criteria for COVID-19 Testing of Heath Care Workers. *Acad. Emerg. Med.* 27 (6), 469–474. doi:10.1111/acem. 14009
- Cohen, J., Vignaux, O., and Jacquemard, F. (2020). Covid-19 in Pregnant Women: General Data from a French National Survey. *Eur. J. Obstet. Gynecol. Reprod. Biol.* 251, 267–268. doi:10.1016/j.ejogrb.2020.06.002
- Department of Health (UK) (2013). HBN 00-09—Infection Control in the Built Environment.
- Dhakal, B., D'Souza, A., Chhabra, S., and Hari, P. (2020). Multiple Myeloma and COVID-19. Leukemia 34 (7), 1961–1963. doi:10.1038/s41375-020-0879-9
- Du, H., Dong, X., Zhang, J. j., Cao, Y. y., Akdis, M., Huang, P. q., et al. (2020). Clinical Characteristics of 182 Pediatric COVID-19 Patients with Different Severities and Allergic Status. *Allergy* 76 (2), 510–532. doi:10.1111/all.14452
- Du, W., Yu, J., Wang, H., Zhang, X., Zhang, S., Li, Q., et al. (2020). Clinical Characteristics of COVID-19 in Children Compared with Adults in Shandong Province, China. *Infection* 48 (3), 445–452. doi:10.1007/s15010-020-01427-2
- Ellington, S., Strid, P., Tong, V. T., Woodworth, K., Galang, R. R., Zambrano, L. D., et al. (2020). Characteristics of Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status—United States, January 22-June 7, 2020. MMWR Morb. Mortal. Wkly. Rep. 69 (25), 769–775. doi:10.15585/mmwr.mm6925a1
- Escors, D., Camafeita, E., Ortego, J., Laude, H., and Enjuanes, L. (2001). Organization of Two Transmissible Gastroenteritis Coronavirus Membrane Protein Topologies within the Virion and Core. J. Virol. 75 (24), 12228–12240. doi:10.1128/JVI.75.24.12228-12240.2001
- Felldin, M., Søfteland, J. M., Magnusson, J., Ekberg, J., Karason, K., Schult, A., et al. (2020). Initial Report from a Swedish High-Volume Transplant Center after the First Wave of the COVID-19 Pandemic. *Transplantation* 105 (1), 108–114. doi:10.1097/TP.00000000003436
- Fernández-Ruiz, M., Andrés, A., Loinaz, C., Delgado, J. F., López-Medrano, F., San Juan, R., et al. (2020). COVID-19 in Solid Organ Transplant Recipients: A Single-Center Case Series from Spain. Am. J. Transpl. 20 (7), 1849–1858. doi:10. 1111/ajt.15929
- Fischer, R. J., Bushmaker, T., Judson, S., and Munster, V. J. (2016). Comparison of the Aerosol Stability of 2 Strains of Zaire Ebolavirus from the 1976 and 2013 Outbreaks. J. Infect. Dis. 214 (S3), S290–S293. doi:10.1093/infdis/jiw193
- Gayam, V., Chobufo, M. D., Merghani, M. A., Lamichhane, S., Garlapati, P. R., and Adler, M. K. (2020). Clinical Characteristics and Predictors of Mortality in African-Americans with COVID-19 from an Inner-city Community Teaching Hospital in New York. J. Med. Virol. 93 (2), 812–819. doi:10.1002/jmv.26306
- Gerba, C. P., Wallis, C., and Melnick, J. L. (1975). Microbiological Hazards of Household Toilets: Droplet Production and the Fate of Residual Organisms. *Appl. Microbiol.* 30 (2), 229–237. doi:10.1128/am.30.2.229-237.1975
- Gonzalez-Lugo, J. D., Bachier-Rodriguez, L., Goldfinger, M., Shastri, A., Sica, R. A., Gritsman, K., et al. (2020). A Case Series of Monoclonal Gammopathy of Undetermined Significance and COVID-19. *Br. J. Haematol.* 190 (3), e130–e133. doi:10.1111/bjh.16906
- Gormley, M., Aspray, T. J., and Kelly, D. A. (2020a). COVID-19: Mitigating Transmission via Wastewater Plumbing Systems. Lancet Glob. Health 8 (5), e643. doi:10.1016/S2214-109X(20)30112-1
- Gormley, M., Kelly, D. A., and Aspray, T. J. (2014). Bio-aerosol Cross-Transmission via the Building Drainage System. Conf. Paper. doi:10.13140/ 2.1.3214.9765
- Gormley, M., Aspray, T. J., and Kelly, D. A. (2020b). Aerosol and Bioaerosol Particle Size and Dynamics from Defective Sanitary Plumbing Systems. *medRxiv*. doi:10.1101/2020.11.01.20223974
- Gormley, M., Aspray, T. J., Kelly, D. A., and Rodriguez-Gil, C. (2017). Pathogen Cross-Transmission via Building Sanitary Plumbing Systems in a Full Scale Pilot Test-Rig. PLoS One 12 (2), e0171556. doi:10.1371/journal.pone.0171556
- Gormley, M., and Beattie, R. (2010). Derivation of an Empirical Frequencydependent Friction Factor for Transient Response Analysis of Water Trap Seals in Building Drainage Systems. *Building Serv. Eng. Res. Tech.* 31 (3), 221–236. doi:10.1177/0143624410364588

- Gormley, M. (2020). SARS-CoV-2: the Growing Case for Potential Transmission in a Building via Wastewater Plumbing Systems. Ann. Intern. Med. 173 (12), 1020–1021. doi:10.7326/M20-6134
- Gormley, M., Templeton, K., Kelly, D., and Hardie, A. (2013). Environmental Conditions and the Prevalence of Norovirus in Hospital Building Drainage System Wastewater and Airflows. *Building Serv. Eng. Res. Tech.* 35 (3), 244–253. doi:10.1177/0143624413485080
- Grimont, F., and Grimont, P. A. D. (2015a). "Serratia," in *Bergey's Manual of Systematics in Archaea and Bacteria*. Editors M. E. Trujillo, P. Dedysh, B. DeVos, B. Hedlund, P. Kampfer, F. A. Rainey, et al. (Hoboken, NJ: John Wiley & Sons, Inc.). doi:10.1002/9781118960608.gbm01167
- Grimont, P. A. D., and Grimont, F. (2015b). "Enterobacter," in *Bergey's Manual of Systematics in Archaea and Bacteria*. Editors M. E. Trujillo, P. Dedysh, B. DeVos, B. Hedlund, P. Kampfer, F. A. Rainey, et al. (Hoboken, NJ: John Wiley & Sons, Inc.). doi:10.1002/9781118960608.gbm01145
- Grimont, P. A. D., and Grimont, F. (2015c). "Klebsiella," in *Bergey's Manual of Systematics in Archaea and Bacteria*. Editors M. E. Trujillo, P. Dedysh, B. DeVos, B. Hedlund, P. Kampfer, F. A. Rainey, et al. (Hoboken, NJ: John Wiley & Sons, Inc.). doi:10.1002/9781118960608.gbm01150
- Guerra, I., Algaba, A., Jiménez, L., Mar Aller, M., Garza, D., Bonillo, D., et al. (2020). Incidence, Clinical Characteristics, and Evolution of SARS-CoV-2 Infection in Patients with Inflammatory Bowel Disease: a Single-Center Study in Madrid, Spain. *Inflam. Bowel Dis.* 27 (1), 25–33. doi:10.1093/ibd/ izaa221
- Han, C., Duan, C., Zhang, S., Spiegel, B., Shi, H., Wang, W., et al. (2020). Digestive Symptoms in COVID-19 Patients with Mild Disease Severity: Clinical Presentation, Stool Viral RNA Testing, and Outcomes. Am. J. Gastroenterol. 115 (6), 916–923. doi:10.14309/ajg.000000000000664
- Han, M. S., Seong, M.-W., Kim, N., Shin, S., Cho, S. I., Park, H., et al. (2020). Viral RNA Load in Mildly Symptomatic and Asymptomatic Children with COVID-19, Seoul, South Korea. *Emerg. Infect. Dis.* 26 (10), 2497–2499. doi:10.3201/ eid2610.202449
- He, Y., Luo, J., Yang, J., Song, J., Wei, L., and Ma, W. (2020). Value of Viral Nucleic Acid in Sputum and Faeces and Specific IgM/IgG in Serum for the Diagnosis of Coronavirus Disease 2019. Front. Cel. Infect. Microbiol. 10, 445. doi:10.3389/ fcimb.2020.00445
- Holshue, M. L., DeBolt, C., Lindquist, S., Lofy, K. H., Wiesman, J., Bruce, H., et al. (2020). First Case of 2019 Novel Coronavirus in the United States. N. Engl. J. Med. 382 (10), 929–936. doi:10.1056/NEJMoa2001191
- Huang, L., Zhang, X., Zhang, X., Wei, Z., Zhang, L., Xu, J., et al. (2020). 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. 80 (6), e1–e13. doi:10.1016/j.jinf.2020.03.006
- Hung, H. C., Chan, D. W., Law, L. K., Chan, E. H., and Wong, E. S. (2006). Industrial Experience and Research into the Causes of SARS Virus Transmission in a High-Rise Residential Housing Estate in Hong Kong. *Building Serv. Eng. Res. Tech.* 27 (2), 91–102. doi:10.1191/0143624406bt1450a
- Hung, I. F., Lung, K. C., Tso, E. Y., Liu, R., Chung, T. W., Chu, M. Y., et al. (2020). Triple Combination of Interferon Beta-1b, Lopinavir-Ritonavir, and Ribavirin in the Treatment of Patients Admitted to Hospital with CoViD-19: An Open-Label, Randomised, Phase 2 Trial. *Lancet* 395 (10238), 1695. doi:10.1016/ S0140-6736(20)31042-4
- Hung, I. F. N., Cheng, V. C. C., Wu, A. K. L., Tang, B. S. F., Chan, K. H., Chu, C. M., et al. (2004). Viral Loads in Clinical Specimens and SARS Manifestations. *Emerg. Infect. Dis.* 10 (9), 1550–1557. doi:10.3201/eid1009.040058
- Hussain, F. A., Njoku, F. U., Saraf, S. L., Molokie, R. E., Gordeuk, V. R., and Han, J. (2020). COVID-19 Infection in Patients with Sickle Cell Disease. Br. J. Haematol. 189 (5), 851–852. doi:10.1111/bjh.16734
- Ishiguro, T., Takano, K., Kagiyama, N., Hosoda, C., Kobayashi, Y., Takaku, Y., et al. (2020). Clinical Course and Findings of 14 Patients with COVID-19 Compared with 5 Patients with Conventional Human Coronavirus Pneumonia. *Respir. Med. Case Rep.* 31, 101207. doi:10.1016/j.rmcr.2020.101207
- Jack, L. B., Cheng, C., and Lu, W. H. (2006). Numerical Simulation of Pressure and Airflow Response of Building Drainage Ventilation Systems. *Building Serv. Eng. Res. Tech.* 27 (2), 141–152. doi:10.1191/0143624406bt1520a

- Jeong, H. W., Kim, S.-M., Kim, H.-S., Kim, Y.-I., Kim, J. H., Cho, J. Y., et al. (2020). Viable SARS-CoV-2 in Various Specimens from COVID-19 Patients. *Clin. Microbiol. Infect.* 26 (11), 1520–1524. doi:10.1016/j.cmi.2020.07.020
- Jin, X., Lian, J.-S., Hu, J.-H., Gao, J., Zheng, L., Zhang, Y.-M., et al. (2020). Epidemiological, Clinical and Virological Characteristics of 74 Cases of Coronavirus-Infected Disease 2019 (COVID-19) with Gastrointestinal Symptoms. Gut 69 (6), 1002–1009. doi:10.1136/gutjnl-2020-320926
- Jones, D. L., Baluja, M. Q., Graham, D. W., Corbishley, A., McDonald, J. E., Malham, S. K., et al. (2020). Shedding of SARS-CoV-2 in Faeces and Urine and its Potential Role in Person-To-Person Transmission and the Environment-Based Spread of COVID-19. *Sci. Total Environ.* 749, 141364. doi:10.1016/j. scitotenv.2020.141364
- Kang, M., Wei, J., Yuan, J., Guo, J., Zhang, Y., Hang, J., et al. (2020). Probable Evidence of Faecal Aerosol Transmission of SARS-CoV-2 in a High-Rise Building. Ann. Intern. Med. 173 (12), 974–980. doi:10.7326/M20-0928
- Kelly, D., Swaffield, J., Jack, L., Campbell, D., and Gormley, M. (2008). Pressure Transient Identification of Depleted Appliance Trap Seals: A Pressure Pulse Technique. *Building Serv. Eng. Res. Tech.* 29 (2), 165–181. doi:10.1177/ 0143624408090202
- Kim, J.-M., Kim, H. M., Lee, E. J., Jo, H. J., Yoon, Y., Lee, N.-J., et al. (2020). 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. 11 (3), 112–117. doi:10.24171/j.phrp.2020.11.3.02
- Kim, S. W., Ramakrishnan, M. A., Raynor, P. C., and Goyal, S. M. (2007). Effects of Humidity and Other Factors on the Generation and Sampling of a Coronavirus Aerosol. Aerobiologia 23 (4), 239–248. doi:10.1007/s10453-007-9068-9
- Kinoshita, T., Bales, R. C., Maguire, K. M., and Gerba, C. P. (1993). Effect of pH on Bacteriophage Transport through Sandy Soils. J. Contaminant Hydrol. 14 (1), 55–70. doi:10.1016/0169-7722(93)90041-P
- Kujawski, S. A., Wong, K. K., Collins, J. P., Epstein, L., Killerby, M. E., Midgley, C. M., et al. (2020). Clinical and Virologic Characteristics of the First 12 Patients with Coronavirus Disease 2019 (COVID-19) in the United States. *Nat. Med.* 26 (6), 861–868. doi:10.1038/s41591-020-0877-5
- Kumar, S., Nyodu, R., Maurya, V. K., and Saxena, S. K. (2020). "Morphology, Genome Organization, Replication, and Pathogenesis of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)," in Coronavirus Disease 2019 (COVID-19). Medical Virology: From Pathogenesis to Disease Control. Editor S. Saxena (Singapore: Springer), 23–31. doi:10.1007/978-981-15-4814-7_3
- Kutter, J. S., de Meulder, D., Bestebroer, T. M., Lexmond, P., Mulders, A., Fouchier, R. A., et al. (2020). SARS-CoV and SARS-CoV-2 Are Transmitted through the Air between Ferrets over More Than One Meter Distance. *bioRxiv*. doi:10.1101/ 2020.10.19.345363
- Lai, A. C. K., Tan, T. F., Li, W. S., and Ip, D. K. M. (2018). Emission Strength of Airborne Pathogens during Toilet Flushing. *Indoor Air* 28 (1), 73–79. doi:10. 1111/ina.12406
- Lau, S. K. P., Che, X.-Y., Woo, P. C. Y., Wong, B. H. L., Cheng, V. C. C., Woo, G. K. S., et al. (2005). SARS Coronavirus Detection Methods. *Emerg. Infect. Dis.* 11 (7), 1108–1111. doi:10.3201/eid1107.041045
- Leung, W. K., To, W-F., Chan, P. K. S., Chan, H. L. Y., Wu, A. K. L., Lee, N., et al. (2003). Enteric Involvement of Severe Acute Respiratory Syndrome-Associated Coronavirus Infection. *Gastroenterology* 125 (4), 1011–1017. doi:10.1016/ s0016-5085(03)01215-0
- Li, J., Chen, Z., Nie, Y., Ma, Y., Guo, Q., and Dai, X. (2020). Identification of Symptoms Prognostic of CoViD-19 Severity: Multivariate Data Analysis of a Case Series in Henan Province. J. Med. Internet Res. 22 (6), e19636. doi:10.2196/ 19636
- Lin, K., and Marr, L. C. (2017). Aerosolisation of Ebola Virus Surrogates in Wastewater Systems. *Environ. Sci. Technol.* 51 (5), 2669–2675. doi:10.1021/acs. est.6b04846
- Lin, L., Jiang, X., Zhang, Z., Huang, S., Zhang, Z., Fang, Z., et al. (2020). Gastrointestinal Symptoms of 95 Cases with SARS-CoV-2 Infection. *Gut* 69 (6), 997–1001. doi:10.1136/gutjnl-2020-321013
- Liu, D., Li, L., Wu, X., Zheng, D., Wang, J., Yang, L., et al. (2020). Pregnancy and Perinatal Outcomes of Women with Coronavirus Disease (COVID-19) Pneumonia: A Preliminary Analysis. Am. J. Roentgenology 215 (1), 127–132. doi:10.2214/AJR.20.23072

- Liu, P., Cai, J., Jia, R., Xia, S., Wang, X., Cao, L., et al. (2020). Dynamic Surveillance of SARS-CoV-2 Shedding and Neutralizing Antibody in Children with COVID-19. *Emerging Microbes & Infections* 9 (1), 1254–1258. doi:10.1080/ 22221751.2020.1772677
- Liu, Y., Ning, Z., Chen, Y., Guo, M., Liu, Y., Gali, N. K., et al. (2020). Aerodynamic Analysis of SARS-CoV-2 in Two Wuhan Hospitals. *Nature* 582 (7813), 557–560. doi:10.1038/s41586-020-2271-3
- Lo, I. L., Lio, C. F., Cheong, H. H., Lei, C. I., Cheong, T. H., Zhong, X., et al. (2020). Evaluation of SARS-CoV-2 RNA Shedding in Clinical Specimens and Clinical Characteristics of 10 Patients with COVID-19 in Macau. *Int. J. Biol. Sci.* 16 (10), 1698–1707. doi:10.7150/ijbs.45357
- Lui, G., Ling, L., Lai, C. K., Tso, E. Y., Fung, K. S., Chan, V., et al. (2020). Viral Dynamics of SARS-CoV-2 across a Spectrum of Disease Severity in COVID-19. *J. Infect.* 81 (2), 318–356. doi:10.1016/j.jinf.2020.04.014
- Magnavita, N., Tripepi, G., and Di Prinzio, R. R. (2020). Symptoms in Health Care Workers during the COVID-19 Epidemic. A Cross-Sectional Survey. *Int.* J. Environ. Res. Public Health 17 (14), 5218. doi:10.3390/ijerph17145218
- Mathian, A., Mahevas, M., Rohmer, J., Roumier, M., Cohen-Aubart, F., Amador-Borrero, B., et al. (2020). Clinical Course of Coronavirus Disease 2019 (COVID-19) in a Series of 17 Patients with Systemic Lupus Erythematosus under Long-Term Treatment with Hydroxychloroquine. *Ann. Rheum. Dis.* 79 (6), 837–839. doi:10.1136/annrheumdis-2020-217566
- Menni, C., Valdes, A. M., Freidin, M. B., Sudre, C. H., Nguyen, L. H., Drew, D. A., et al. (2020). Real-time Tracking of Self-Reported Symptoms to Predict Potential COVID-19. *Nat. Med.* 26 (7), 1037–1040. doi:10.1038/s41591-020-0916-2
- Moore, B., Perry, C. E. L., and Chard, S. T. (1952). A Survey by the Sewage Swab Method of Latent Enteric Infection in an Urban Area. J. Hyg. 50, 137–156. doi:10.1017/s0022172400019501
- Moore, G., Hewitt, M., Stevenson, D., Walker, J. T., and Bennett, A. M. (2015). Aerosolisation of Respirable Droplets from a Domestic Spa Pool and the Use of MS-2 Coliphage and *Pseudomonas aeruginosa* as Markers for *Legionella pneumophila*. *Appl. Environ. Microbiol.* 81 (2), 555–561. doi:10.1128/AEM. 02912-14
- Morrow, A. W. (1969). Concentration of the Virus of Foot and Mouth Disease by Foam Flotation. *Nature* 222 (5192), 489–490. doi:10.1038/222489a0
- Muenchhoff, M., Mairhofer, H., Nitschko, H., Grzimek-Koschewa, N., Hoffmann, D., Berger, A., et al. (2020). Multicentre Comparison of Quantitative PCR-Based Assays to Detect SARS-CoV-2, Germany, March 2020. *Euro Surveill*. 25 (24), 2001057. doi:10.2807/1560-7917.ES.2020.25.24.2001057
- Nature (2020). Coronavirus in the Air. Media. Available at: nature.com/ original/magazine-assets/d41586-020-02058-1/d41586-020-02058-1.pdf. (Accessed November 30 2020).
- Newsom, S. W. B. (1972). Microbiology of Hospital Toilets. Lancet 300 (7779), 700–703. doi:10.1016/S0140-6736(72)92102-2
- Nowak, B., Szymański, P., Pańkowski, I., Szarowska, A., Życińska, K., Rogowski, W., et al. (2020). Clinical Characteristics and Short-Term Outcomes of Coronavirus Disease 2019: Retrospective, Single-Center Experience of Designated Hospital in Poland. *Pol. Arch. Intern. Med.* 130 (5), 407–411. doi:10.20452/pamw.15361
- Palaiodimos, L., Kokkinidis, D. G., Li, W., Karamanis, D., Ognibene, J., Arora, S., et al. (2020). Severe Obesity, Increasing Age and Male Sex Are Independently Associated with Worse In-Hospital Outcomes, and Higher In-Hospital Mortality, in a Cohort of Patients with COVID-19 in the Bronx, New York. *Metabolism* 108, 154262. doi:10.1016/j.metabol.2020.154262
- Palleroni, N. J. (2015). "Pseudomonas," in *Bergey's Manual of Systematics in Archaea and Bacteria*. Editors M. E. Trujillo, P. Dedysh, B. DeVos, B. Hedlund, P. Kampfer, F. A. Rainey, et al. (Hoboken, NJ: John Wiley & Sons, Inc.). doi:10. 1002/9781118960608.gbm01210
- Pan, L., Mu, M., Yang, P., Sun, Y., Wang, R., Yan, J., et al. (2020). Clinical Characteristics of COVID-19 Patients with Digestive Symptoms in Hubei, China: a Descriptive, Cross-Sectional, Multicenter Study. Am. J. Gastroenterol. 115 (5), 766–773. doi:10.14309/ajg.000000000000020
- Park, S.-K., Lee, C.-W., Park, D.-I., Woo, H.-Y., Cheong, H. S., Shin, H. C., et al. (2020). Detection of SARS-CoV-2 in Faecal Samples from Patients with Asymptomatic and Mild COVID-19 in Korea. *Clin. Gastroenterol. Hepatol.* doi:10.1016/j.cgh.2020.06.005
- Patel, J. (2020). Faecal Shedding of SARS-CoV-2: Considerations for Hospital Settings. J. Hosp. Infect. 105 (4), 782–783. doi:10.1016/j.jhin.2020.05.019

- Peiris, J. S. M., Chu, C. M., Cheng, V. C. C., Chan, K. S., Hung, I. F. N., Poon, L. L. M., et al. (2003). Clinical Progression and Viral Load in a Community Outbreak of Coronavirus-Associated SARS Pneumonia: a Prospective Study. *Lancet* 361 (9371). 1767–1772. doi:10.1016/S0140-6736(03)13412-5
- Peng, L., Liu, J., Xu, W., Luo, Q., Chen, D., Lei, Z., et al. (2020). SARS-CoV-2 Can Be Detected in Urine, Blood, Anal Swabs, and Oropharyngeal Swabs Specimens. J. Med. Virol. 92 (9), 1676–1680. doi:10.1002/jmv.25936
- Penner, J. L. (2015). "Proteus," in Bergey's Manual of Systematics in Archaea and Bacteria. Editors M. E. Trujillo, P. Dedysh, B. DeVos, B. Hedlund, P. Kampfer, F. A. Rainey, et al. (Hoboken, NJ: John Wiley & Sons, Inc.). doi:10.1002/9781118960608.gbm01162
- Polo, D., Quintela-Baluja, M., Corbishley, A., Jones, D. L., Singer, A. C., Graham, D. W., et al. (2020). Making Waves: Wastewater-Based Epidemiology for COVID-19 Approaches and Challenges for Surveillance and Prediction. *Water Res.* 186, 116404. doi:10.1016/j.watres.2020.116404
- Popoff, M. Y., and le Minor, L. E. (2015). "Salmonella," in *Bergey's Manual of Systematics in Archaea and Bacteria*. Editors M. E. Trujillo, P. Dedysh, B. DeVos, B. Hedlund, P. Kampfer, F. A. Rainey, et al. (Hoboken, NJ: John Wiley & Sons, Inc.). doi:10.1002/9781118960608.gbm01166
- Rainey, F. A., Hollen, B. J., and Small, A. M. (2015). "Clostridium," in *Bergey's Manual of Systematics in Archaea and Bacteria*. Editors M. E. Trujillo, P. Dedysh, B. DeVos, B. Hedlund, P. Kampfer, F. A. Rainey, et al. (Hoboken, NJ: John Wiley & Sons, Inc.). doi:10.1002/9781118960608. gbm00619
- Remes-Troche, J. M., Ramos-de-la-Medina, A., Manríquez-Reyes, M., Martínez-Pérez-Maldonado, L., Lara, E. L., and Solís-González, M. A. (2020). Initial Gastrointestinal Manifestations in Patients with Severe Acute Respiratory Syndrome Coronavirus 2 Infection in 112 Patients from Veracruz in Southeastern Mexico. *Gastroenterology* 159 (3), 1179–1181. doi:10.1053/j. gastro.2020.05.055
- Ridgway, J. P., Farley, B., Benoit, J.-L., Frohne, C., Hazra, A., Pettit, N., et al. (2020). A Case Series of Five People Living with HIV Hospitalised with COVID-19 in Chicago, Illinois. *AIDS Patient Care and STDs* 34 (8), 331–335. doi:10.1089/apc. 2020.0103
- Romero, J. R., and Modlin, J. F. (2015). "Introduction to the Human Enteroviruses and Parechoviruses," in *Mandell, Douglas, and Bennett's Principles and Practice* of Infectious Diseases. 8th Edn, Editor J. E. Bennett, R. Dolin, M. J. Blaser, and W. B. Saunders (Philadelphia, PA: Elsevier Saunders), 2066–2072.e2. 9781455748013. doi:10.1016/B978-1-4557-4801-3.00172-7
- Sachdeva, M., Uppal, N. N., Hirsch, J. S., Ng, J. H., Malieckal, D., Fishbane, S., et al. (2020). COVID-19 in Hospitalised Patients on Chronic Peritoneal Dialysis: a Case Series. Am. J. Nephrol. 51 (8), 669–674. doi:10.1159/000510259
- Salanueva, I. J., Carrascosa, J. L., and Risco, C. (1999). Structural Maturation of the Transmissible Gastroenteritis Coronavirus. J. Virol. 73 (10), 7952–7964. doi:10. 1128/JVI.73.10.7952-7964.1999
- Scheutz, F., and Strockbine, N. A. (2015). "Escherichia," in *Bergey's Manual of Systematics in Archaea and Bacteria*. Editors M. E. Trujillo, P. Dedysh, B. DeVos, B. Hedlund, P. Kampfer, F. A. Rainey, et al. (Hoboken, NJ: John Wiley & Sons, Inc.). doi:10.1002/9781118960608.gbm01147
- Schlottau, K., Rissmann, M., Graaf, A., Schön, J., Sehl, J., Wylezich, C., et al. (2020). SARS-CoV-2 in Fruit Bats, Ferrets, Pigs, and Chickens: an Experimental Transmission Study. *Lancet: Microbe* 1 (5), e218–e225. doi:10.1016/S2666-5247(20)30089-6
- Shang, H., Bai, T., Chen, Y., Huang, C., Zhang, S., Yang, P., et al. (2020). Outcomes and Implications of Diarrhoea in Patients with SARS-CoV-2 Infection. Scand. J. Gastroenterol. 55 (9), 1049–1056. doi:10.1080/ 00365521.2020.1800078
- Shi, J., Wen, Z., Zhong, G., Yang, H., Wang, C., Huang, B., et al. (2020). Susceptibility of Ferrets, Cats, Dogs, and Other Domesticated Animals to SARS-Coronavirus 2. *Science* 368 (6494), 1016–1020. doi:10.1126/science.abb7015
- Smither, S. J., Eastaugh, L. S., Findlay, J. S., and Lever, M. S. (2020). Experimental Aerosol Survival of SARS-CoV-2 in Artificial Saliva and Tissue Culture Media at Medium and High Humidity. *Emerging Microbes & Infections* 9 (1), 1415–1417. doi:10.1080/22221751.2020.1777906
- Strockbine, N. A., and Maurelli, A. T. (2015). "Shigella," in *Bergey's Manual of Systematics in Archaea and Bacteria*. Editors M. E. Trujillo, P. Dedysh, B. DeVos, B. Hedlund, P. Kampfer, F. A. Rainey, et al. (Hoboken, NJ: John Wiley & Sons, Inc.). doi:10.1002/9781118960608.gbm01168

- Swaffield, J. A., Campbell, D. P., and Gormley, M. (2005a). Pressure Transient Control: Part I - Criteria for Transient Analysis and Control. *Building Serv. Eng. Res. Tech.* 26 (2), 99–114. doi:10.1191/0143624405bt1190a
- Swaffield, J., Campbell, D., and Gormley, M. (2005b). Pressure Transient Control: Part II-Simulation and Design of a Positive Surge Protection Device for Building Drainage Networks. *Building Serv. Eng. Res. Tech.* 26 (3), 195–212. doi:10.1191/0143624405bt1200a
- Taxonera, C., Sagastagoitia, I., Alba, C., Mañas, N., Olivares, D., and Rey, E. (2020). 2019 Novel Coronavirus Disease (COVID-19) in Patients with Inflammatory Bowel Diseases. *Aliment. Pharmacol. Ther.* 52 (2), 276–283. doi:10.1111/apt. 15804
- Tschopp, J., L'Huillier, A. G., Mombelli, M., Mueller, N. J., Khanna, N., Garzoni, C., et al. (2020). First Experience of SARS-CoV-2 Infections in Solid Organ Transplant Recipients in the Swiss Transplant Cohort Study. Am. J. Transpl. 20 (10), 2876–2882. doi:10.1111/ajt.16062
- Vacchiano, V., Riguzzi, P., Volpi, L., Tappatà, M., Avoni, P., Rizzo, G., et al. (2020). Early Neurological Manifestations of Hospitalised COVID-19 Patients. *Neurol. Sci.* 41 (8), 2029–2031. doi:10.1007/s10072-020-04525-z
- van Doremalen, N., Bushmaker, T., Morris, D. H., Holbrook, M. G., Gamble, A., Williamson, B. N., et al. (2020). Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. N. Engl. J. Med. 382 (16), 1564–1567. doi:10. 1056/NEJMc2004973
- Wang, F., Yang, Y., Dong, K., Yan, Y., Zhang, S., Ren, H., et al. (2020). Clinical Characteristics of 28 Patients with Diabetes and CoViD-19 in Wuhan, China. *Endocr. Pract.* 26 (6), 668–674. doi:10.4158/EP-2020-0108
- Wang, R., He, H., Liao, C., Hu, H., Hu, C., Zhang, J., et al. (2020). Clinical Outcomes of Hemodialysis Patients Infected with Severe Acute Respiratory Syndrome Coronavirus 2 and Impact of Proactive Chest Computed Tomography Scans. *Clin. Kidney J.* 13 (3), 328–333. doi:10.1093/ckj/sfaa086
- Wang, W., Xu, Y., Gao, R., Lu, R., Han, K., Wu, G., et al. (2020). Detection of SARS-CoV-2 in Different Types of Clinical Specimens. *JAMA* 323 (18), 1843–1844. doi:10.1001/jama.2020.3786
- Wang, X., Zheng, J., Guo, L., Yao, H., Wang, L., Xia, X., et al. (2020). Faecal Viral Shedding in COVID-19 Patients: Clinical Significance, Viral Load Dynamics and Survival Analysis. *Virus. Res.* 289, 198147. doi:10.1016/j.virusres.2020. 198147
- Wei, X.-S., Wang, X., Niu, Y.-R., Ye, L.-L., Peng, W.-B., Wang, Z.-H., et al. (2020). Diarrhoea Is Associated with Prolonged Symptoms and Viral Carriage in Corona Virus Disease 2019. *Clin. Gastroenterol. Hepatol.* 18 (8), 1753–1759. doi:10.1016/j.cgh.2020.04.030
- WHO (2020). Coronavirus Disease (COVID-19): How Is it Transmitted? Available at: www.who.int/news-room/q-a-detail/coronavirus-disease-covid-19-how-isit-transmitted (Accessed November 30, 2020).
- Wilson, N., Corbett, S., and Tovey, E. (2020). Airborne Transmission of Covid-19. BMJ 370, m3206. doi:10.1136/bmj.m3206
- Wölfel, R., Corman, V. M., Guggemos, W., Seilmaier, M., Zange, S., Müller, M. A., et al. (2020). Virological Assessment of Hospitalised Patients with COVID-2019. *Nature* 581 (7809), 465–469. doi:10.1038/s41586-020-2196-x
- Wu, Y., Guo, C., Tang, L., Hong, Z., Zhou, J., Dong, X., et al. (2020a). Prolonged Presence of SARS-CoV-2 Viral RNA in Faecal Samples. *Lancet Gastroenterol. Hepatol.* 5 (5), 434–435. doi:10.1016/S2468-1253(20)30083-2
- Wu, Y.-T., Liu, J., Xu, J.-J., Chen, Y.-F., Yang, W., Chen, Y., et al. (2020). Neonatal Outcome in 29 Pregnant Women with COVID-19: A Retrospective Study in Wuhan, China. *Plos Med.* 17 (7), e1003195. doi:10.1371/journal.pmed.1003195
- Wu, Y., Liu, F., Fang, Y., Lu, X., Wu, Y., Xia, L., et al. (2020b). A Report of Clustered COVID-19 in a Hematology Ward. *Blood Adv.* 4 (12), 2736–2738. doi:10.1182/ bloodadvances.2020001982
- Xagoraraki, I., Yin, Z., and Syambayev, Z. (2020). Fate of Viruses in Water Systems. J. Environ. Eng. 140 (1), 04014020. doi:10.1061/(ASCE)EE.1943-7870.0000827
- Xiao, F., Sun, J., Xu, Y., Li, F., Huang, X., Li, H., et al. (2020a). Infectious SARS-CoV-2 in Faeces of Patient with Severe COVID-19. *Emerg. Infect. Dis.* 26 (8), 1920–1922. doi:10.3201/eid2608.200681

- Xiao, F., Tang, M., Zheng, X., Liu, Y., Li, X., and Shan, H. (2020b). Evidence for Gastrointestinal Infection of SARS-CoV-2. Gastroenterology 158 (6), 1831–1833. doi:10.1053/j.gastro.2020.02.055
- Xiao, Y., Huang, S., Yan, L., Wang, H., Wang, F., Zhou, T., et al. (2020). Clinical Characteristics of Diarrhoea in 90 Cases with COVID-19: A Descriptive Study. *Int. Emerg. Nurs.* 52, 100912. doi:10.1016/j.ienj.2020.100912
- Xiong, X.-l., Wong, K. K.-y., Chi, S.-q., Zhou, A.-f., Tang, J.-q., Zhou, L.-s., et al. (2020). Comparative Study of the Clinical Characteristics and Epidemiological Trend of 244 COVID-19 Infected Children with or without GI Symptoms. *Gut* 70 (2), 436–438. doi:10.1136/gutjnl-2020-321486
- Xu, X., and Weisel, C. P. (2005). Human Respiratory Uptake of Chloroform and Haloketones during Showering. J. Expo. Sci. Environ. Epidemiol. 15 (1), 6–16. doi:10.1038/sj.jea.7500374
- Yan, C. H., Faraji, F., Prajapati, D. P., Boone, C. E., and DeConde, A. S. (2020). Association of Chemosensory Dysfunction and COVID-19 in Patients Presenting with Influenza-like Symptoms. *Int. Forum Allergy Rhinol.* 10 (7), 806–813. doi:10.1002/alr.22579
- Yin, S., Peng, Y., Ren, Y., Hu, M., Tang, L., Xiang, Z., et al. (2020). The Implications of Preliminary Screening and Diagnosis: Clinical Characteristics of 33 Mild Patients with SARS-CoV-2 Infection in Hunan, China. J. Clin. Virol. 128, 104397. doi:10.1016/j.jcv.2020.104397
- Young, B. E., Ong, S. W. X., Kalimuddin, S., Low, J. G., Tan, S. Y., Loh, J., et al. (2020). Epidemiologic Features and Clinical Course of Patients Infected with SARS-CoV-2 in Singapore. *JAMA* 323 (15), 1488–1494. doi:10.1001/jama.2020. 3204
- Yu, N., Li, W., Kang, Q., Xiong, Z., Wang, S., Lin, X., et al. (2020). 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.* 20 (5), 559–564. doi:10.1016/S1473-3099(20)30176-6
- Zhang, C., Gu, J., Chen, Q., Deng, N., Li, J., Huang, L., et al. (2020). Clinical and Epidemiological Characteristics of Pediatric SARS-CoV-2 Infections in China: a Multicenter Case Series. *Plos Med.* 17 (6), e1003130. doi:10.1371/journal.pmed. 1003130
- Zhang, H., Liao, Y.-S., Gong, J., Liu, J., Xia, X., and Zhang, H. (2020). Clinical Characteristics of Coronavirus Disease (CoViD-19) Patients with Gastrointestinal Symptoms: a Report of 164 Cases. *Dig. Liver Dis.* 52 (10), 1076–1079. doi:10.1016/j.dld.2020.04.034
- Zhang, L., Mei, Q., Li, L., Ye, C., Huang, Y., Wang, Y., et al. (2020b). [Analysis of Gastrointestinal Symptoms in 80 Patients with Coronavirus Disease 2019]. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue* 32 (4), 412–416. doi:10.3760/cma.j. cn121430-20200406-00411
- Zhang, L., Han, C., Zhang, S., Duan, C., Shang, H., Bai, T., et al. (2020a). Diarrhoea and Altered Inflammatory Cytokine Pattern in Severe Coronavirus Disease 2019: Impact on Disease Course and In-hospital Mortality. J. Gastroenterol. Hepatol. 36 (2), 421–429. doi:10.1111/jgh.15166
- Zheng, S., Fan, J., Yu, F., Feng, B., Lou, B., Zou, Q., et al. (2020). Viral Load Dynamics and Disease Severity in Patients Infected with SARS-CoV-2 in Zhejiang Province, China, January-March 2020: Retrospective Cohort Study. *BMJ* 369, m1443. doi:10.1136/bmj.m1443
- Zhou, Y. Y., Benson, C., Irvin, Y.-S., Irshad, H., and Cheng, Y. S. (2007). Particle Size Distribution and Inhalation Dose of Shower Water under Selected Operating Conditions. *Inhalation Toxicol.* 19 (4), 333–342. doi:10.1080/ 08958370601144241

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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