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Pit latrines may be a potential risk in rural China and low-income countries when dealing with COVID-19

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HIGHLIGHTS
• Live SARS-CoV-2 was isolated from COVID-19 patients’ excreta.
• Pit latrines and using untreated excreta as fertilizer are common in rural areas.
• SARS-CoV-2 RNA particles were detected in wastewater.
• SARS-CoV-2 spilled from pit latrines might be a sustainable source of infection.
• Toilets revolution may prevent COVID-19 and other potential waterborne diseases.

GRAPHICAL ABSTRACT

ABSTRACT

According to the latest reports, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which caused coronavirus disease 2019 (COVID-19), was successfully isolated from the excreta (stool and urine) of COVID-19 patients, suggesting SARS-CoV-2 could be transmitted through excreta contaminated water. As pit latrines and the use of untreated excreta as fertilizer were common in rural China, we surveyed 27 villages of Jiangxi and Hubei provinces and found that pit latrines could be a potential source of SARS-CoV-2 water pollution. Recently, bats have been widely recognized as the source of SARS-CoV-2. There were many possible intermediate hosts of SARS-CoV-2, including pangolin, snake, bird and fish, but which one was still not clear exactly. Here, we proposed a hypothesis to illustrate the mechanism that SARS-CoV-2 might spread from the excreta of infected humans in pit latrines to potential animal hosts, thus becoming a sustainable source of infection in rural China. Therefore, we believe that abolishing pit latrines and banning the use of untreated excreta as fertilizer can improve the local living environment and effectively prevent COVID-19 and other potential waterborne diseases that could emanate from the excreta of infected persons. Although this study focused on rural areas in China, the results could also be applied to low-income countries, especially in Africa.

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1. Introduction

The ongoing pandemic of coronavirus disease 2019 (COVID-19) is an emerging respiratory infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which was named 2019-nCoV previously (Zhu et al., 2020), posing an unprecedented challenge to global public health. The most common symptoms of COVID-19 patients include fever (80%–99%, 90% on average), cough (59%–82%, 69%
on average), fatigue (70%), sore throat (5%–40%, 21% on average), shortness of breath (31%–55%, 39% on average), rhinorrhea (4%–20%, 12% on average) and muscle ache (11%–35%, 23% on average) (Cai et al., 2020; Chen et al., 2020a; Huang et al., 2020; Wang et al., 2020a), while diarrhea (2%–10%, 5% on average), nausea (10%), vomiting (4%) and abdominal pain (2%) were also reported (Huang et al., 2020, Chen et al., 2020a, Wang et al., 2020a). Significantly, SARS-CoV-2 ribonucleic acid (RNA) was detected in the stool of 53%–83% (64% on average) COVID-19 patients (including patients with severe symptoms, asymptomatic status, and treated patients with no further sign of the symptoms), and the duration of positive stool ranged from one day to more than a month (Cai et al., 2020; Chen et al., 2020b; Holshue et al., 2020; Lescure et al., 2020; Pan et al., 2020; Tang et al., 2020; Wang et al., 2020b; Wu et al., 2020c; Xiao et al., 2020a; Xu et al., 2020; Zheng et al., 2020). Among all patients, 23%–43% (33% on average) of all age groups and 80% of children were still positive in stool even after the respiratory tract samples were negative (Chen et al., 2020b; Wu et al., 2020c; Xiao et al., 2020a; Xu et al., 2020), suggesting that SARS-CoV-2 might be excreted from gastrointestinal tract and the fecal-oral transmission was possible (Cai et al., 2020; Gao et al., 2020; Xiao et al., 2020a). To investigate the possibility of enteric infection by SARS-CoV-2 as reported previously in severe acute respiratory syndrome coronavirus (SARS-CoV) and middle east respiratory syndrome coronavirus (MERS-CoV) infections (Leung et al., 2003; Zhou et al., 2017), Zhou et al. (2020a) isolated SARS-CoV-2 from differentiated bat small intestinal organoids and human intestinal organoids, an in vitro model of the human intestinal epithelium. They found that both bat and human intestinal organoids developed progressive cytopathic changes after SARS-CoV-2 inoculation and accompanied by a substantially increased viral load in the culture media (Zhou et al., 2020a), suggesting that active replication of SARS-CoV-2 in human intestinal organoids. Notably, infectious SARS-CoV-2 was successfully isolated from the stool specimen of a patient with diarrheal COVID-19 (Zhou et al., 2020a) and 2 patients without diarrhea (Wang et al., 2020d). Another study showed that infectious SARS-CoV-2 virus were successfully isolated from 2 of 3 patients with viral RNA-positive, indicating that infectious virus in feces was a common manifestation of COVID-19 and confirmed the potential of fecal-oral or fecal–respiratory transmission (Xiao et al., 2020b). In addition, recent studies showed that human angiotensin-converting enzyme II (ACE2), which had been proved to be a cell receptor for SARS-CoV-2 (Lu et al., 2020; Zhou et al., 2020b), was highly expressed in glandular cells of human gastric, duodenal, and rectal epithelia, supporting the entry of SARS-CoV-2 into host cells (Xiao et al., 2020a). Moreover, viral nucleocapsid protein (NP)-positive cells were not only observed in the cytoplasm of gastric, duodenal, and rectum glandular epithelial cells from the biopsy specimens of COVID-19 patients (Xiao et al., 2020a), but also in human intestinal organoids (Zhou et al., 2020a). Collectively, the available evidence demonstrated that the occurrence of SARS-CoV-2 infection in human intestinal organoids might recapitulate enteric infection of COVID-19 patients, and the human intestinal tract might represent an additional route for SARS-CoV-2 transmission (Zhou et al., 2020a). In the meantime, SARS-CoV-2 RNA was also detected in the urine sample (Sun et al., 2020), sink, and toilet (Ong et al., 2020) of COVID-19 patients, and the positive urine duration was more than one month (Sun et al., 2020). Notably, Sun et al. (2020) successfully isolated infectious SARS-CoV-2 from the urine of a COVID-19 patient, suggesting that SARS-CoV-2 might be secreted through the human urinary system.

Considering that infectious SARS-CoV-2 virus was found in urine and stool samples from COVID-19 patients on days 11–15 of the clinical process (Jeong et al., 2020), and the duration of SARS-CoV-2 RNA positive in stool and urine would last more than one month (Cai et al., 2020; Chen et al., 2020b; Holshue et al., 2020; Lescure et al., 2020; Pan et al., 2020; Tang et al., 2020; Wang et al., 2020b; Wu et al., 2020c; Xiao et al., 2020a; Xu et al., 2020; Zheng et al., 2020; Sun et al., 2020), we believed that SARS-CoV-2 might exist in the stool and urine of patients with COVID-19 for a long time. According to the available literature, SARS-CoV-2 RNA was detected in wastewater samples from the Netherlands (Lodder and de Roda Husman, 2020), Australia (Ahmed et al., 2020), France (Wurtzer et al., 2020), USA (Wu et al., 2020a), Italy (La Rosa et al., 2020b), and Spain (Randazzo et al., 2020), we inferred that SARS-CoV-2 contaminated water might be a potential sustainable source of infection, thus threatening the local individuals’ health. Previous studies have shown that water contaminated by bacteria, viruses, and chemicals was closely related to the use of pit latrines and septic tanks (Gerba, 1999; Graham and Polizzotto, 2013; Hammoud et al., 2018; Ngasala et al., 2019). Herein, this study aims to comprehensively evaluate the potential risks of COVID-19 in rural China through the investigation of rural geographical environment, the use of pit latrines, and the villagers’ daily life, then try to find out the solutions. Although this study focused on rural areas in China, the results could also be applied to other low-income countries, especially in Africa.

2. Materials and methods

2.1. Field survey

In order to prevent the spread of COVID-19, several versions of the prevention guidelines were issued in China, suggesting that people with a history of living or traveling in epidemic areas should carry out self-health monitoring twice a day for 14 days from the time of leaving the epidemic area, and try to live alone or in a single room with good ventilation to minimize close contact with their families (National Health Commission of the People's Republic of China, 2020). In addition, we also conducted a detailed survey on the distribution of family houses and daily life routes of villagers with a history of being COVID-19 patients at the epicenter of the Wuhan epidemic to identify the impact of pit latrines on the risks of COVID-19 transmission.

A field investigation was carried out in 3 villages of Jiangxi province, China, which contained returnees from Wuhan. The survey included the sources of domestic water, the structure, distribution and use of pit latrines among villages, and the excreta management pattern in rural China, to find out whether there was a systematic disinfection process and analyze the possibility of fecal contamination of drinking water. In addition, we also conducted a detailed survey on the distribution of family houses and daily life routes of villagers with a history of being in epidemic areas in Wuhan and other cities of Hubei province to identify the impact of pit latrines on the risks of COVID-19 transmission.

2.2. Source of data

Village committees are grass-roots mass organizations of self-governance elected by villagers of the administrative village under the jurisdiction of a township in mainland China, a village committee shall be composed of 3–7 members, including the chairman, vice-chairmen and members (Chinese Government, 2010). Their functions mainly include self-management, self-education, self-service by villagers, and carry out democratic elections, democratic decision-making, democratic management and democratic supervision. The village committees handle the village’s public affairs and public welfare undertakings, mediate civil disputes, assist in maintaining public order, and report to the people’s government the opinions, requirements and suggestions of the villagers (Chinese Government, 2010). Thus, the village committees know the basic situation of the village very well.
To understand the prevalence of pit latrines in rural China, we contacted to the village committees from 27 villages in Jiangxi and Hubei provinces by phone, email and WeChat to survey the number of households, the total population, the average household size, whether there are flush toilets at family, whether villagers use pit latrines, and whether villagers use untreated excreta as fertilizer among the rural households. Here, we define flush toilets as flushing human excreta (urine and feces) into the septic-tanks through drainpipes, and then the excreta in septic-tanks can be made harmless by bacterial fermentation or centralized disinfection when necessary (for example: to kill potential SARS-CoV-2). This definition is consistent with the Joint Monitoring Programme (JMP) classification of improved sanitation facilities that flush or pour flush toilets connecting to piped sewers systems (WHO and UNICEF, 2017).

3. Results and discussions

3.1. Pit latrines and excreta management in rural China

Chinese villages have long been known for their small bridges and flowing water, which means that Chinese villages are usually built near streams, where great rivers originated. During the field investigation of 3 villages in Jiangxi province, China, we found that they all located upstream of the river, and many pit latrines are scattered around the rural houses throughout the villages. As shown in Fig. 1, a typical pit latrine in rural China consists of 3 main parts: a shelter for creating a private space, a slab or floor with a small hole for villagers to defecate, and a cesspool for storing feces and urine. Besides, there was usually a small window on the wall of cesspool for farmers to take the excreta as a natural fertilizer. To make it easier for farmers to get the excreta, some cesspools were built on the open next to the shelter. As described in available researches (Heinonen-Tanski and van Wijk-Sijbesma, 2005; Lam et al., 2020a; Mamera et al., 2020), human urine and feces as fertilizer could meet the needs of plants for potassium and phosphorus, and improve soil structure, and using human excreta as fertilizer is free, which leads to the villagers like to use excreta as fertilizer. Through surveying 27 villages in Jiangxi and Hubei provinces by contacting the village committees through phone, email and WeChat, it was found that about 0%-60% (31% on average) of rural households used the excreta directly from the pit latrines as crop fertilizer in recent 3 years. In addition, according to the villagers, we learned that the excreta in the open cesspools may be washed to everywhere by rainwater, or be carried to everywhere by animal like dogs, cats, or field mouse, eventually polluting the local water. Fortunately, the villagers’ domestic water is all diverted from the mountain stream by water pipes rather than groundwater. Although the water from mountain stream was not treated before using, it was not polluted by excreta as the source of water was far away from the pit latrines.

It was well documented that the bacteria, viruses, and chemicals within drinking water sources or agricultural soil posed a great threat to human health (Gerba, 1999; Gerba and Bitton, 1984; Graham and Polizzotto, 2013; Hammoud et al., 2018; Jamieson et al., 2002; Leung et al., 2020; Mamera and Van Tol, 2018; Mamera et al., 2020; Nganje et al., 2020; Tallon et al., 2005). For example, wells in nearby septic tanks and pit latrines were found to be significantly contaminated in Dar es Salaam, Tanzania, leading to more than 80% of wells contained with *Escherichia coli* and 58% of wells with nitrate levels higher than WHO guidelines (Ngasala et al., 2019). It has been recognized that the consequent movement of pathogens along with subsurface drainage systems to surface water systems was the main route of pathogen transport (Jamieson et al., 2002; Prüss-Ustün et al., 2019), and it was possible that slimy bacteria form a thin coat over the pipelines to aid in the spread of SARS-CoV-2 (Naddeo and Lii, 2020). Thus, SARS-CoV-2, as a virus, may also be transmitted through water.

A study from Australia (Ahmed et al., 2020) showed that the number of infected individuals in the catchment areas could be reasonably estimated by detecting the copy numbers of SARS-CoV-2 RNA in the wastewater, which verified that early detection of coronavirus in wastewater might be a viable surveillance strategy for COVID-19 infections (Daughton, 2020; Orive et al., 2020; Wu et al., 2020) as previously demonstrated for hepatitis A virus, norovirus (Hellmér et al., 2014) and poliovirus (Asghar et al., 2014; Lodder et al., 2012). Although there was no sufficient evidence that fecal-oral transmission of COVID-19 was viable, while there was evidence showed that SARS-CoV-2 could be easily and sustainably transmitted in the community in Shenzhen, China, because the proportion of COVID-19 patients without definitive exposure from January 25 through February 5 (11%) was much higher than that before January 24 (6%) (Liu et al., 2020). This suggests that there may be other potential routes of transmission, such as exposure to SARS-CoV-2 that survive in community environment. Given that the infectious SARS-CoV-2 was found to be secreted through the human urinary system (Sun et al., 2020) and intestinal tract (Wang et al., 2020d; Xiao et al., 2020b; Zhou et al., 2020a), and SARS-CoV-2 RNA was detected in wastewater worldwide (Randazzo et al., 2020), many studies have suggested the possibility of wastewater transmission of COVID-19 disease (Adelodun et al., 2020; Arslan et al., 2020; Foladori et al., 2020). However, the direct use of untreated excreta as a fertilizer and the flushing of excreta from open cesspools into the waters on rainy days might lead to serious water pollution, including the SARS-CoV-2 within human excreta. Thus, the possibility of SARS-CoV-2 transmission through water contaminated with human excreta cannot be ignored.

3.2. SARS-CoV-2 survives in nature could be a potentially sustainable source of infection

Coronaviruses are present in a variety of animals and can cause respiratory, enteric, hepatic, and nervous system diseases of varying severity (Lau et al., 2005). The members of the coronavirus family, SARS-CoV (Drosten et al., 2003), MERS-CoV (Chan et al., 2015) and the current SARS-CoV-2 (Zhu et al., 2020) have caused severe respiratory illness and high mortality to humans since 2002. Studies have shown that both SARS-CoV and MERS-CoV were likely originated from bats and then crossed species barriers to infect humans through an amplification mammalian host, the *Panguma larvata* for SARS-CoV and the *Camelus dromedarius* for MERS-CoV (Chan et al., 2015; Cheng et al., 2007; Lii et al., 2005). Similarly, recent studies have shown that SARS-CoV-2 might originated from bats with the genome of SARS-CoV-2 has 88%-96% (91% on average) nucleotide identity with several

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**Fig. 1.** Schematic diagram of a typical pit latrine in rural China.
bat coronaviruses and 79%–82% (80% on average) with human SARS-CoV, but might with more proximal origins from a potential intermediate animal host (Chan et al., 2020; Ji et al., 2020; Lu et al., 2020; Zhou et al., 2020b). It has been reported that pangolins (Lam et al., 2020b; Lopes et al., 2020; Wahba et al., 2020; Xiao et al., 2020c; Zhang et al., 2020b) and snakes (Ji et al., 2020) might be the intermediate hosts of SARS-CoV-2. However, the possibility of snakes as intermediate hosts of SARS-CoV-2 was questioned by the scientific community (Zhang et al., 2020b), and the existing evidence was not sufficient to either confirm or rule out the role of pangolins as an intermediate host (Tiwari et al., 2020; Wahba et al., 2020). In other words, it is still not clear which animal is the intermediate hosts that brings SARS-CoV-2 to human hosts.

Bats and birds are natural reservoirs for providing coronavirus and influenza virus genes during the evolution of new virus species and viruses for interspecies transmission (Chan et al., 2013). As described in the latest review (Tiwari et al., 2020), many coronaviruses have bats, birds, or pigs as the primary host, in addition to infecting animals such as civets, pangolins, and camels, coronaviruses also could be harbored by a range of animal species, such as fish, snake, cattle, horse, dog, cat, rabbit, rodent, ferret, minks, frog, marmot, and hedgehog. Moreover, Damas et al. (2020) had greatly expanded the potential number of intermediate hosts that might be infected by SARS-CoV-2 through ACE2 receptors by protein structural analysis, which means that plenty of wild animals might be novel SARS-CoV-2 hosts. The results highlight the importance of wildlife and biosecurity in farms and wet markets, which may serve as the potential source and amplification centers for emerging infections (Cheng et al., 2007; Tiwari et al., 2020).

Previous studies have elucidated that SARS-CoV could survive for 4 days in diarrheal stool samples with an alkaline pH (Lai et al., 2005), 14 days in sewage at 4 degrees Celsius and 2 days at 20 degrees Celsius (Wang et al., 2005), and retained its viability for over 5 days at temperatures of 22 °C–25 °C and relative humidity of 40%–50% (Chan et al., 2011). Kampf et al. (2020) analyzed 22 studies and found that human coronaviruses such as SARS-CoV, MERS-CoV or endemic human coronaviruses could persist on inanimate surfaces like metal, glass or plastic for up to 9 days. Another study (Casanova et al., 2009) found that two surrogate coronaviruses, transmissible gastroenteritis (TGEV) and mouse hepatitis (MHV) remained infectious in water and sewage for days to weeks at 25 degrees Celsius, the time for 99% reduction was 9 days for TGEV and 7 days for MHV even in the pasteurized settled sewage, suggesting that contaminated water might a potential vehicle for human exposure if aerosol was generated. Notably, recent studies demonstrated that SARS-CoV-2 was highly stable at 4 °C with only around a 0.7 log-unit reduction of infectious titre on day 14, but was sensitive to heat as the time for virus inactivation was reduced to 5 min (Chin et al., 2020). Besides, no infectious virus was detected from treated smooth surfaces on day 4 (glass and banknote) or day 7 (stainless steel and plastic), but a detectable level of infectious virus could still be present on the outer layer of a surgical mask on day 7 (Chin et al., 2020). SARS-CoV-2 could be highly stable in a favorable environment (van Doremalen et al., 2020), for example, SARS-CoV-2 is extremely stable in a wide range of pH values at room temperature (pH 3–10) (Chin et al., 2020).

Infectious SARS-CoV-2 has been found in human excreta samples of COVID-19 patient in many previous studies (Sun et al., 2020; Wang et al., 2020d; Xiao et al., 2020b; Zhou et al., 2020a), and the SARS-CoV-2 embedded in stool particles in septic tanks could escape from disinfection and slowly release into aqueous phase, behaving as a secondary source of SARS-CoV-2 and potentially contributing to its spread through drainage pipelines (Zhang et al., 2020c). Former study has found that particles (kaolin clay, humic acid powder, and activated sludge) <2 μm in diameter were large enough to protect viruses from 254-nm ultraviolet (UV) light (Templeton et al., 2005), suggesting that the protection of fecal particles might make the survival of SARS-CoV-2 more easier. The SARS-CoV-2 within the excreta of COVID-19 patients can be released into the water (natural environment) (Zhang et al., 2020c) when farmers use untreated excreta as fertilizer in agricultural fields, and the excreta been washed into water by rainwater or be carried to water by animal. Then the SARS-CoV-2 survived in the natural

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Fig. 2. SARS-CoV-2 may spread from the excreta of infected humans in pit latrines to potential animal hosts and then become a sustainable source of infection. Detailed description in the text.
environment would be available absorbed by wild animals (such as bats, birds, fishes, and snakes) by drinking or contacting contaminated water, and become a secondary source of human SARS-CoV-2 infection. This hypothesis was consistent with another study that SARS-CoV-2 spilled into novel wild hosts in North America, as demonstrated by Franklin and Bevins (2020) through a conceptual model for the perpetuation of the pathogen. Owing to the typically high mutation rates of RNA viruses, coronaviruses (including SARS-CoV-2) can rapidly increase their virulence and adapt to new hosts (Duffy, 2018; Elena and Sanjuán, 2005). Besides, the potential aquatic animals that may be infected with SARS-CoV-2 in the river may reach cities downstream of the river, then may be caught and eaten by city dwellers, further expanding the range of transmission. As excreta was directly used as fertilizer, fruits and vegetables grown in rural areas might be contaminated by SARS-CoV-2 and then eaten by wild animals, or purchased and eaten by rural and urban residents through wet markets. Long-term exposure to contaminated environmental sources, such as the air pollutants, extended exposure to aerosols produced by contaminated water, and become a secondary source of human SARS-CoV-2 infection.

Fig. 3. The population situation and the prevalence of pit latrines in rural China. The top row was the total population of each village, the middle row was the average household size of each village, the bottom row was the proportion of households using flush toilets or using pit latrines.
many countries, such as social distancing, handwashing, mask-wearing, isolation, quarantine, and community containment (Ataguba and Ataguba, 2020; Mahase, 2020; Teslya et al., 2020; Wilder-Smith and Freedman, 2020), and these measures were effective and have been confirmed by multiple reports (Mwalili et al., 2020; Ngonghala et al., 2020; Teslya et al., 2020; Tian et al., 2020).

Table 1
The population situation in rural China and the proportion of households with or without flush toilets.

| Villages in rural China | Num of households | Total population | Average household size | Num of the households using flush toilets | Percent of the households using flush toilets | Num of the households using pit latrines | Percent of the households using pit latrines |
|------------------------|-------------------|------------------|-----------------------|------------------------------------------|---------------------------------------------|------------------------------------------|---------------------------------------------|
| 1                      | 235               | 1146             | 4.876595745           | 193                                      | 0.821276596                                 | 42                                       | 0.178723404                                 |
| 2                      | 225               | 795              | 3.533333333           | 178                                      | 0.791111111                                 | 47                                       | 0.208888889                                 |
| 3                      | 237               | 481              | 2.029535865           | 119                                      | 0.502109705                                 | 118                                      | 0.497890295                                 |
| 4                      | 422               | 1201             | 2.845971564           | 190                                      | 0.450236967                                 | 232                                      | 0.549763033                                 |
| 5                      | 412               | 1213             | 2.94174757            | 132                                      | 0.32038835                                  | 280                                      | 0.67961105                                 |

During the field investigation of 3 villages in Jiangxi province, China, we found that it was common for villagers to live with scattered houses and share pit latrines, with 1 to 5 households (an average of 2.2) sharing one pit latrines. As shown in Fig. 4, of the 8 households in A–H, only household A included a member with a history of being in epidemic areas (Wuhan), family members of both C and H households all...
defecated in pit latrines, other households' members defecated in flush toilets at their home and occasionally used the pit latrines. The houses of A, B, and C households were scattered, naturally, the daily life routes of family members were significantly larger than those of other families. Notably, the use of pit latrines expanded the daily life routes of C and H households' members and increased the possibility of close contact and exposure to SARS-CoV-2 between individuals. Ultimately, it might increase the risk of COVID-19 transmission. Given that plentiful household-shared toilet facilities (most of them were pit latrines) with poor ancillary facilities (such as hand-washing facilities) were common in low-income countries (Antwi-Agyei et al., 2020; Ssemugabo et al., 2020), we believed that the use of pit latrines in rural China and low-income countries would increase the contact between human, thus increasing the risk of COVID-19 transmission to a certain extent.

4. Conclusion

We proposed this hypothesis to illustrate the mechanism that SARS-CoV-2 might spread from the excreta of infected humans in pit latrines to potential animal hosts and then become a sustainable source of infection in rural China and other low-income countries. The widely use of pit latrines and open cesspools coupled with agricultural fields application of untreated excreta could act as a potential route for the spread of COVID-19 disease and other possible waterborne diseases that could emanate from the excreta of infected persons. We suggest for further implementation of the toilets revolution in rural China and also low-income countries in the world, completely replace pit latrines by flush toilets. Next, according to the division of the residential area, using drainage systems to collect human excreta centrally and then used as agricultural fertilizer after unified disinfection treatment. Through these preventive measures, the local living environment will be significantly improved and SARS-CoV-2 and other potential waterborne diseases will be effectively prevented.

CRediT authorship contribution statement

Lilong Liu, Junyi Hu, and Yaxin Hou contributed equally to this work.

Lilong Liu: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Roles/WRiting - original draft. Junyi Hu: Data curation, Formal analysis, Investigation, Methodology, Roles/WRiting - original draft. Yaxin Hou: Investigation, Methodology. Zhen Tao: Conceptualization, Investigation, Methodology, Writing - review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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