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The SARS-CoV-2 outbreak from a One Health perspective

Maged Gomaa Hemida^{1, 2*} and Mohammed M Ba Abdullah³

¹Department of Microbiology, College of Veterinary Medicine, King Faisal University, Saudi Arabia

²Department of Virology, Faculty of Veterinary Medicine, Kafrelsheikh University, Egypt

³Department of Biological Sciences, College of Science, King Faisal University, Saudi Arabia

*Corresponding author

CRedit author statement

Dr. Maged Gomaa Hemida: the first and corresponding author of this manuscript. He conceived the idea, gathered the ideas, collect the data from various sources, drafted the manuscript, analysed the data and oversee the submission and

Dr. Mohamed Ba Abdullah: he helped with conceiving the idea, did the sequencing analysis, drafted the manuscript, and revision of this manuscript.

Abstract

The SARS-CoV-2 is a new human coronavirus candidate recently detected in China that is now reported in people on inhabited continents. The virus shares a high level of identity with some bat coronaviruses and is recognised as a potentially zoonotic virus. We are utilizing the One Health concept to understand the emergence of the virus, as well as to point to some possible control strategies that might reduce the spread of the virus across the globe; thus, containment of such virus would be possible.

Keywords: SARS-CoV, SARS-CoV-2, CoVID-19, MERS CoV coronavirus, Outbreak, One Health, bats, animal, reservoir

The severe acute respiratory syndrome-2 was named the coronavirus infectious diseases-19 (CoVID-19). However, it was called the novel coronavirus at the beginning of this outbreak. This virus was provisionally named 2019-nCoV at the very beginning of its emergence in China, after emerging in China in late 2019 [1]. Since that time, there has been an escalation in the number of confirmed cases, notably from China, but also in more than 113 countries and territories around the globe.

Historically four coronaviruses candidates (HCoV-229E, HCoV-OC43, HCoV-NL63, and HCoV-UKU1), causing common cold or flu-like symptoms were known. Patients infected by these viruses usually recover spontaneously in a short time [2]. The SARS-CoV-2 is the seventh coronavirus known to infect humans, appearing in less than ten years since the emergence of Middle East respiratory syndrome coronavirus (MERS-CoV) in late 2012 and SARS-CoV in 2003 [3, 4]. This virus belongs to the family *Coronaviridae*; a large group of viruses that have the potential to infect and cause diseases to a large number of mammals, birds as well as humans. Members of this family cause a wide variety of clinical signs in their affected hosts, including respiratory, enteric, nervous, and systemic health problems. The viral genomes of coronaviruses have many unique features that make them prone to frequent coding changes, thus generating new candidates in a short period [5]. The reasons behind this rapid mutational frequency are the poor proofreading capability of the viral RNA polymerase and the possibility of recombination between various members of this family [6]. Recent studies showing the (angiotensin-converting enzyme A, (ACE-2)), ACE-2 is the primary receptors for the SARS-CoV-2 and other candidates of the B lineage of the Beta coronaviruses [7]. High expression levels of some potential viral receptors in many hosts from mammals, birds in addition to humans make them susceptible to

the virus infection. In recent studies, it is apparent that SARS-CoV-2 uses the mechanism that SARS-CoV used for cell entry. The mechanism of the virus entry to the cell resulting from the interaction between the virus receptors and the spike glycoprotein, after priming of that viral protein by the Serine protease TMPRSS2 [8]. Further, inhibition of TMPRSS2, blocked cell entry by SARS-CoV-2, indicating similar or identical pathways for cell invasion and possible strategies for therapeutics [8]. The WHO declared the virus as a global health emergency on Jan 31, 2020 [9]. As of 10 AM CET 03 March 2020, there are 128920 laboratory-confirmed cases reported to the WHO from 113 countries and territories across the globe with a total fatality of 4747 [10]. Currently, the case fatality rate is relatively low ($\approx 3.6\%$) compared to infections with severe acute respiratory syndrome coronavirus (SARS-CoV, (10%) and MERS-CoV (32%) [11]. The numbers of infected and dead persons are much higher than the latter viruses. However, these numbers will be subject to changes with the newly reported cases and the outcomes of the ongoing active human cases. During mid February 2020, a new criterion for the patient identification has been launched considering the chest Computed Tomography (CT) scans to identify patients suffering from respiratory distresses. [12] The reasons behind the switch from the detection of the viral nucleic acids by real-time PCR to CT scanning at that time for patient identification are (i) to give a chance to all patients to get the proper care at the right time (ii) the variation in the incubation period of the viral infection among various people (iii) the possibility of super-spreader of the virus who shed the virus to the environment in large numbers and poses a great risk of infection to the close contact people. This phenomenon have been reported previously in Ebola, virus, SARS-CoV, MERS-CoV, and recently in SARS-CoV-2 [13-15]. Using some mathematical tools models late Feb, 2020, the basic reproduction (R_0) to the human-to-human transmission was around 3.58. However, the same study found the R_0 for the bat-to-

human was 2.30 [16]. Based on these findings, the R_0 of SARS-CoV-2 was almost close to SARS-CoV but higher than MERS-CoV, with the exception of the MERS-CoV outbreak in South Korea [16].

Some putative One Health-based insights for the evolution and spread of SARS-CoV-2

The MERS-CoV and the SARS-CoV-2 are both considered airborne pathogens [17] with a tendency to transmit through the aerosol of infected patients. The human-to-human nosocomial transmission was recently reported, which is contributing substantially to the spreading and sustainability of the virus. Some family clusters were also recently reported inside China [18]. The incubation period of the diseases ranges from 2- 14 days post-infection [19, 20]. The asymptomatic individuals may play essential roles in the spread of the virus within a specific community [21]. However, there are ongoing debates about the possibility of infected persons to shed the virus early during the course of an infection with this virus even before the appearance of the clinical signs [20, 22]. The emergence of the virus was believed to be linked with some human cases who suffered from severe pneumonia, which have a relation with a wet animal Huanan Seafood Wholesale market in Wuhan, China (1). These observations, along with the sequence identity of the virus, have drawn attention to the likely zoonotic origin of the virus. The SARS-CoV-2 infection is potentially another important example of the One Health concept, after SARS-CoV, MERS-CoV, and Ebola virus, in which there is an excellent overlapping in human, animal, and environmental health [23]. The full-length genome of the virus was recently made available to the scientific community [20]. This sequence will have a significant impact on the development of novel diagnostic assays, antiviral drugs, and vaccines against the virus soon. Interestingly, the virus genome and its spike glycoprotein showing 96.11 % and 92.86 identities to the *Rhinolophus affinis* bat coronavirus, respectively (Table 1), from Wuhan, China (RaTG13,

accession number MN996532.1) recently deposited in the Genbank [24]. Bats are representing almost one-fourth of the mammalian population [25]. They are widely distributed all over the world in all continents except Antarctica [25]. Bats are classified under the order Chiroptera that are found more than 50 million years ago. This order includes more than 1300 species of bats [25]. Several studies suggested that bats are the common reservoir for the SARS-CoV were the sequences for viruses isolated from Chinese horseshoe bats shared a high degree of identity with SARS-CoV [26]. Metagenomics paved the way for the discovery of a large number of viruses in different species, including bats. There are more than 200 coronaviruses have been identified in various species of bats [27]. The main bat reservoirs of the SARS-CoV was identified in 2003 [28]. Meanwhile, several species of bats including, *Taphous perforatus*, *Rhinopoma hardwickii*, and *Pipistrellus kuhlii* were believed to be the ancestors for the MERS-CoV [29]. Based on the previous emergence history of SARS-CoV, the presence of a large number of mammals and birds overcrowded in one place may give a chance for pathogens, particularly those with RNA genomes such as coronaviruses and influenza viruses, to emerge. However, it remains uncertain whether a similar emergence for SARS-CoV-2 can be postulated. One potential reservoir of SARS-CoV was the Palm Civet cat (*Paguma larvata*), a member of the *Viverridae*, a group of mammals found in Asia [30]. SARS-CoV was able to infect and replicated efficiently in these animals [31]. Serosurveillance for the antibodies against SARS-CoV in workers from one wild animal market in Guangzhou was conducted in 2006 [32]. This study showed the presence of specific IgG antibodies against SARS-CoV in these workers where the civet cats were available [32]. This same study confirmed the hypothesis of the implication of civet cats in the emergence and sustainability of SARS-CoV at that time. The identification of this reservoir was one of the milestones in control and containment of SARS-CoV (9), and

subsequent banning of the trade of civet cats in the wild animal market was a significant step toward the containing of SARS-CoV [33]. This approach highlights the roles of One Health in controlling such zoonotic pathogens. Based on the evidence gained from studies of SARS-CoV, and from the genetic identity of SARS-CoV-2, it could be postulated that the virus responsible for the recent outbreak is transmitted from bats to humans either directly or indirectly through adaptation in an unidentified host [34, 35].

Some potential One Health strategies for the control of SARS-CoV-2

The one health concept could be the most logical approach in case of fighting and control some zoonotic pathogens, especially those who do not have available medication or vaccines during an epidemic or outbreak. There are many aspects by which the one health concept may contribute substantially to the control of the current SARS-CoV-2 outbreak. Adoption of some of one health-based control strategies was of great success in controlling MERS-CoV, contributing at least in part to the decline in the case fatality rates from 52% in 2012 to 32% in 2020 in case of MERS-CoV [23, 36]. Similar approaches were also successful in containing some of the highly pathogenic avian influenza viruses [37]. In the following sections, we are suggesting some One Health-based control strategies for the containment of SARS-CoV-2 (Figure 2).

Some control strategies based on the physicochemical and biological properties of coronaviruses

Coronaviruses are enveloped viruses like influenza, HIV, rabies etc, their envelope composed of a lipid bilayer, which the virus acquires from the host cell membrane while releasing from the infected cells [38]. Using lipid solvents and detergents was proved to inactivate SARS-CoV through permeant damage of the lipid components of the viral envelope [39]. This study showed

a drastic drop in the viral titer after one-minute treatment [39]. This raises the mandate of hand as well as personal hygiene as one of the gold standard control measures for not only coronaviruses but also for most enveloped viruses. Coronaviruses are small, approximately 100-120 nm in diameter. This is making them able to pass the pores of the surgical masks very easily. Thus, wearing special masks with minute pore sizes like N95 could be one of the preventive measures against respiratory pathogens, including influenza and coronaviruses, in comparison to another type of masks [40, 41]. However, the WHO already indicated certain rules for wearing the N95 masks, particularly for the health care workers and people in close contact with active cases [42]. The genome of coronaviruses is composed of single-strand positive-sense RNA molecules. The virus genome acts as a mRNA and is infectious. The ultraviolet light has harmful effects on the SARS-CoV genome when used at 254 nm wavelength for 60 minutes [43, 44]. Meanwhile, the effect of temperature on the virus infectivity/survival has great impact on the control of this class of respiratory viruses. SARS-CoV may live in the environment at average room temperature about 22 °C for 2hrs without losing its infectivity. However, the virus infectivity is greatly affected by exposure to 56°C for at least 30 min [44]. These parameters have great roles in the virus control as we discuss below. As mentioned above, the coronavirus genomes are prone to frequent changes due to many factors; a new study highlighted the presence of two variants (L and S) of the SARS-CoV-2. This study confirmed that variant L (more severe) was dominant during the early outbreak in China, which was responsible for at least 70% of the cases at that time. However, the implementation of drastic control measures against the virus posed some selective pressure on this variant then the S variant becomes the predominant at this time [45]. Thus, frequent monitoring of the virus on the genomic level is highly encouraged. Meanwhile,

the preparation of vaccine and antiviral drugs should be done from the most recent generation and seeds of the circulating strains and variants of the virus to ensure high efficacy rates.

Meanwhile, there is an urgent need for the development of novel diagnostic assays that enable the early detection of the virus, even in low copy numbers in the patient specimens. Detection of cases during the early stage of the infection could be a crucial step in the early identification of the infected person; thus, proper treatment and control should be in place as early as possible. Furthermore, the development of multiplex diagnostic assays that enable the detection of the most common respiratory pathogen in one reaction is highly recommended. It would be of high value to develop novel diagnostic tests that distinguish the seven human coronaviruses in one reaction per sample. This unique approach may help in screening a large number of people and animals and will have a significant impact on the fast track testing of travelers from at-risk regions.

Strategies based on animal-human interaction

Both SARS-CoV and MERS-CoV have zoonotic origins in which the Civet Cats and dromedary camels played important roles in the sustainability and transmission of these viruses in the community as well as spill over to the human [30, 46]. To identify the animal reservoirs in the context of SARS-CoV and MERS-CoV, scientist screened a large number of animals and birds to identify the main reservoir for those two viruses [47, 48]. SARS-CoV-2 was believed to be originated in people who came in close contact with the live wet market in Wuhan, China, late 2019 [22]. In the case of SARS-CoV-2, recent studies used the informational spectrum tools to identify and predict the actual reservoir, the virus receptors as well as potential therapeutic and vaccine targets [49]. The Wuhan wet market was hosting a large number of wild animals, birds, reptiles, and amphibians which never exist in one location in nature [50]. Simply, there is a close

human-animal contact in the supply chain of these wild animal markets starting from hunting, transporting, selling, processing, including slaughtering, and cooking. This is in addition to the exposure of people to their blood, secretions, and excretions. This chain poses a great risk for the contact between human and these wild animals, which may put the handlers at risk of infection not only for coronaviruses but also for other pathogens that these animals and birds may harbor. In the light of the One Health concept, control of this emerging virus requires the reduction of the viral shedding to the environment from the main reservoirs, for animal-person transmission and from humans for person-person transmission [35]. Based on the previous experience from the other emerging diseases, particularly SARS-CoV and influenza viruses, avoiding the mixing of various species of animals, birds, and mammals, is highly suggested [51, 65, 66]. This strategy will minimize the possibility of recombination among not only these pathogens but also for other common pathogens in the near future. A large number of bats may also be available in this particular market, including the *Rhinolophus affinis*. The viral genome of the bat coronavirus from this particular species was close to the SARS-CoV-2 (Table 1). This result is suggesting these bats are the main ancestor of this virus. About 49% of the first reported human cases had a various level of contact with this market [22]. A recent study showed that Pangolin could be one of the potential intermediate hosts of SARS-CoV-2 [45]. However, this requires further confirmation. Based on the experience from SARS-CoV and MERS-CoV, SARS-CoV-2 could be adapted to humans in a non-identified host, including animals or birds before spilled over to the human. Identification of the intermediate host or reservoir for the SARS-CoV-2, if any, could be one of the milestones of the combating of this virus. This could be done in two consecutive steps. First, conduct a large scale serological testing of the animals and birds sold in this market immediately before this epidemic. This surveillance will give an

idea if particular animals or birds reacted to the virus and carry specific antibodies against it. Second, if seroconversion is proved in any of these animals or birds, testing specimens and tissues from these animals or birds must be carried out to detect the virus in these animals. The live poultry markets were responsible for the transmission of many viral pathogens to humans, especially various types of avian influenza viruses [37, 51, 52]. Several studies reported that banning the storage of live poultry in live markets at least for a short period of time for overnight drastically reduced the ability to isolate the avian influenza viruses by 84% compared with the standard procedures [51]. Another study showed a drastic decrease in the number of reported human cases of avian influenza H7N9 by almost 97% after the closure of live poultry markets in four major provinces in China [53]. Thus, banning the live wild animal trading could have substantial effects on the control strategies not only for coronaviruses but also for other pathogens such as avian influenza viruses. Regular monitoring of the dynamic changes of coronavirus in different species of bats is highly recommended.

Strategies based on the animal/human/environment interaction

The environment serves as the intermediate vessels between the animals and humans. The environmental factors that may contribute to the spread of the virus include air, water, soil, etc. Coronaviruses are airborne viruses that produce nosocomial infections [54]. They are mainly transmitted through droplet infection [55]. When the virus released from the animals or humans, it passes through the air and may drop on some surfaces or objects. Some respiratory pathogens with pandemic potential such as H1N1, SARS-CoV, and MERS-CoV may remain viable in the environment for a longer time up to months on these objects until picked up with another person to contaminate the mucous membranes through touching the nose, mouth or eyes [56]. There are several factors that control the virus's survival in the environment on these objects, such as the

temperature, the relative humidity, the strain of the virus [56]. Some coronaviruses such as HCoV-229E and MERS-CoV were detected on some environmental surfaces during some outbreaks [57, 58]. One of the critical control measures in the case of airborne infection is to develop novel assays that enable us to detect and estimate the virus concentration in the air. This approach will have great implications, especially in the health care settings. The process of decontamination of the virus-contaminated surfaces by the appropriate disinfectants or virucidal agents was successful in case of other respiratory viruses such as SARS-CoV and avian influenza [59]. The hydrogen peroxide vapor showed great success in the decontamination of surfaces contaminated with SARS-CoV and avian influenza viruses [59]. The WHO suggested using two different alcohol-based formulas in the disinfection of enveloped viruses, especially ZIKA, Ebola, SARS-CoV, and MERS-CoV. The second formula (II) was showing excellent results in the disinfection process of the enveloped viruses when compared to the formula (I) [60]. These formulae could be a potential virucidal agent against SARS-CoV-2. This may help in the large-scale decontamination and disinfection of regions where the virus spread, including streets, hospitals, factories, public transportation, parks, worship places, and schools. The environment plays some essential roles in the transmissibility of the virus, as suggested by the correlation between the role of public transportation through the domestic buses, trains, even luxurious cruise ships, and the rate of the reported human SARS-CoV-2 cases [66]. These public transportations like trains, buses, and planes require thorough disinfection between uses.

Strategies based on minimizing virus spread from human-to-human

The significant burden in controlling the respiratory viruses is how to manage the person-to-person transmission. This could be adopted through many strategies. First, personal and hand hygiene are the gold standard approach toward minimizing the possibility of infection for

individuals. This can be achieved by washing the hands with the antiseptics and or soaps and water for at least 30 seconds as per the WHO guidelines [61]. This approach will reduce the virus load in the contaminated hands from virus droplets, which might touch the nose or mouth of persons. Second, practice extreme caution by applying a social distance of at least one meter between you and anyone who is coughing or sneezing [61]. Third, educate the public on how to avoid the frequent touching of the mucous membranes, especially those of nose, mouth, and eyes [61]. Fourth, respiratory protection and hygiene through wearing the most appropriate personal protective equipment, as suggested earlier, according to the WHO's standards [61]. Fifth, vomiting and diarrhea were reported in many SARS-CoV-2 patients [62]. This is suggesting the possibility of the fecal oral route as a mode of transmission of the virus [62]. This stresses out the importance of hand hygiene to avoid any possible transmission of the virus through the fecal oral route. Sixth, one of the main pillars in the control of virus spreads is the identification of the infected personnel. It is one of the crucial steps toward reducing the virus spread in a community. The earlier the identification and detection of the positive cases, the better the control of these cases. Thus, they will receive the better health care treatment and avoid virus spread particularly during the very early stage of the infection. Seventh, special attention should be paid to how to protect the health care workers dealing with active cases. They should provide by the standard PPE and wear them all the time during handling patients or coming in a close contact with infected personnel. Identification of the infected patients as early as possible and tracing his contact with regular monitoring and testing remains the gold standard approach for minimizing the spread of the virus in certain community. Regular monitoring of the circulating air and the cooling systems will help to trace back any circulating virus in a particular region. Eighth, the main current challenges facing the containment of the virus is the spread of the virus via

traveling. Special precautions should be implemented during the travel of the citizens from one country to another especially these countries with a high number of reported cases. Although physical examination through the thermal cameras that help identifying the people suffering from fever is helpful in identifying some potential cases, it may not be necessary that every person suffering from fever is an infected person. On the other hand, some patients did not show any symptoms during the early stage of infection. Additional quick tests should be implemented to identify some potential cases. However, this may require further equipments and designated places in every airport to conduct such measures, at least during the outbreak. This will help in reducing the potential introduction of positive cases to a certain country or provinces within a country in case of quarantine measures. More research is essential to unravel many unknown aspects of the virus evolution, transmission cycle, pathogenesis, and control. Special attention should be directed toward understanding the high transmissibility rate of SARS-CoV-2 compare to other coronaviruses like SARS-CoV and MERS-CoV.

Strategies based on the development of novel vaccines and antiviral therapeutics

One of the most significant obstacles facing the control of SARS-CoV and other coronaviruses such as MERS-CoV is the absence of any licensed vaccine or even medication available for prophylactic and treatment purposes. However, there is an ongoing race among scientists and pharmaceutical companies to develop these useful pharmaceutical preparations for controlling SARS-CoV-2 across the globe. There are many vaccine candidates currently in the clinical trials, while others are still under testing. One strategy for the development of coronavirus recombinant vaccines is to map the neutralizing epitopes within the spike glycoprotein of the virus, express them *in vitro* then use the expressed protein as a vaccine. These vaccines usually trigger the host cell immune response to produce specific antibodies against the virus; thus, protection against

any potential natural infection may be achieved. These strategies will help in the protection of an at-risk group of people, particularly the immunocompromised and people suffering from chronic diseases. The regular monitoring of various coronaviruses, especially in various species of bats, animals, and birds on the genomic level, is highly recommended. Some studies suggested the most human coronaviruses; including SARS-CoV, MERS-CoV, HCoV-229E, and HCoV-NL63 originated from bats [25, 65]. This highlights the mandate for continuous monitoring of the coronaviruses population in bats as an alarm to the emergence of new novel coronaviruses in the future. Second, there is ongoing research to develop antiviral therapy that might help in the treatment of the active human cases of the SARS-CoV-2. Each approach mainly depends on a unique strategy to halt the virus replication or disrupt it at a certain point; thus, the virus cannot complete its replication cycle in the host. Therefore, it reduces the possibility of virus shedding from the infected patients to its close contacts. A recent study used some serine protease TMPRSS2 inhibitors to prevent the virus from entry to the cell. These compounds are clinically approved and potentially will reduce the virus replication [8]. Some FDA approved anthelmintic compounds such as niclosamide have potent antiviral effects not only for SARS-CoV-2 but also for other viruses, including SARS-CoV, MERS-CoV, Zika virus, and HCV [63]. A recent study showed the great values of the Remdesivir (GS-5734) for prophylactic as well as treatment for the MERS-CoV in the rhesus macaque model [64]. This approach could be a promising trend for the prevention and treatment of SARS-CoV-2; however, further studies are required to confirm these findings. Another method was to use the nucleotide analog inhibitors, such as the remdesivir, which targets the viral polymerase (RNA dependant RNA polymerase). This approach diminished the ability of the virus to copy its genome; thus, the replication cycle

may be interrupted. This compound gave promising results in the cell culture model, which requires further testing in laboratory animals before the clinical trials [65].

Conclusions

Although SARS-CoV-2 is rapidly transmitting across the globe, it may be contained if sincere containment measures are implemented. The drastic drop in the number of reported cases in China, along with a reduction in the reported deaths could be an indicator of an early containment of the virus. Implementing the One health concept from all aspects involving the animal, environment, and humans could contribute substantially to the control of SARS-CoV-2 in the near future.

Conflict of interest

The authors declare there is no conflict of interest.

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Tables

Table 1: Pairwise sequence identities between the SARS-CoV-2 (NC_045512.2) and other coronaviruses

Accession No.	Virus	Isolate	Whole-genome	S gene	RBD*
MN996532.1	Bat-CoV	RaTG13	96.11	92.86	86.21

MG772933.1	Bat-SARS-CoV like	Bat-SL-CoVZC45	87.65	75.13	73.05
MG772934.1	Bat-SARS-CoV like	Bat-SL-CoVZXC21	87.43	74.69	72.9
AY390556.1	SARS-CoV	GZ02	78.95	72.56	72.6
NC_004718.3	SARS-CoV	Tor2	78.9	72.54	72.6
AY278489.2	SARS-CoV	GD01	78.9	72.54	64.82
AY278488.2	SARS-CoV	BJ01	78.89	72.48	63.17
JX869059.2	MERS-CoV	EMC	48.83	41.95	38.15

* RBD: receptors binding domains

Figure legends

Figure 1: Proposed diagram for the evolution, spreading and some potential one-health-based control measures for the SARS-CoV-2

The SARS-CoV-2 is most likely originated from unidentified hosts or bats, which play essential roles in the sustainability and spreading of the virus into the environment. The infection may transmit directly from bats to humans or indirectly through an intermediate host/s such as mammals and birds. The virus may be adapted in this unidentified reservoir and transmitted to a human. The main control measures are mainly based on blocking the virus release from the original hosts, including the bats, thus reduce the possibility of human infection. The one health-based control measures mainly depend on stopping or reduction of the virus spreading from the potential reservoirs as well as shedding from human to human. Green arrows mean it confirmed

while red arrow means under investigation. The (x) sign indicates blocking the pathways to stop the virus shedding and thus spreading in a particular community.

Figure 2: Some control interventions for the SARS-CoV -2 based on the One Health concept

Some potential control measures for the SARS-CoV-2 outbreak. (a) Some strategies based on the physicochemical and biological properties of the virus (b) Some strategies based on the animal/human interaction (c) Some strategies based on the animal/environment/human interaction (d) some strategies bases on reduction the virus spread from person to person.

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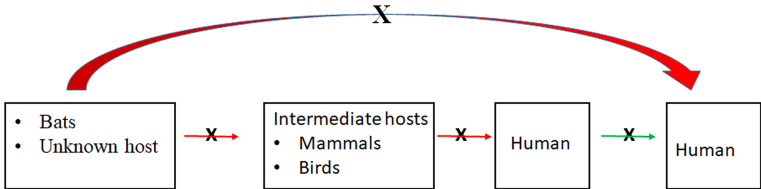


Figure 1

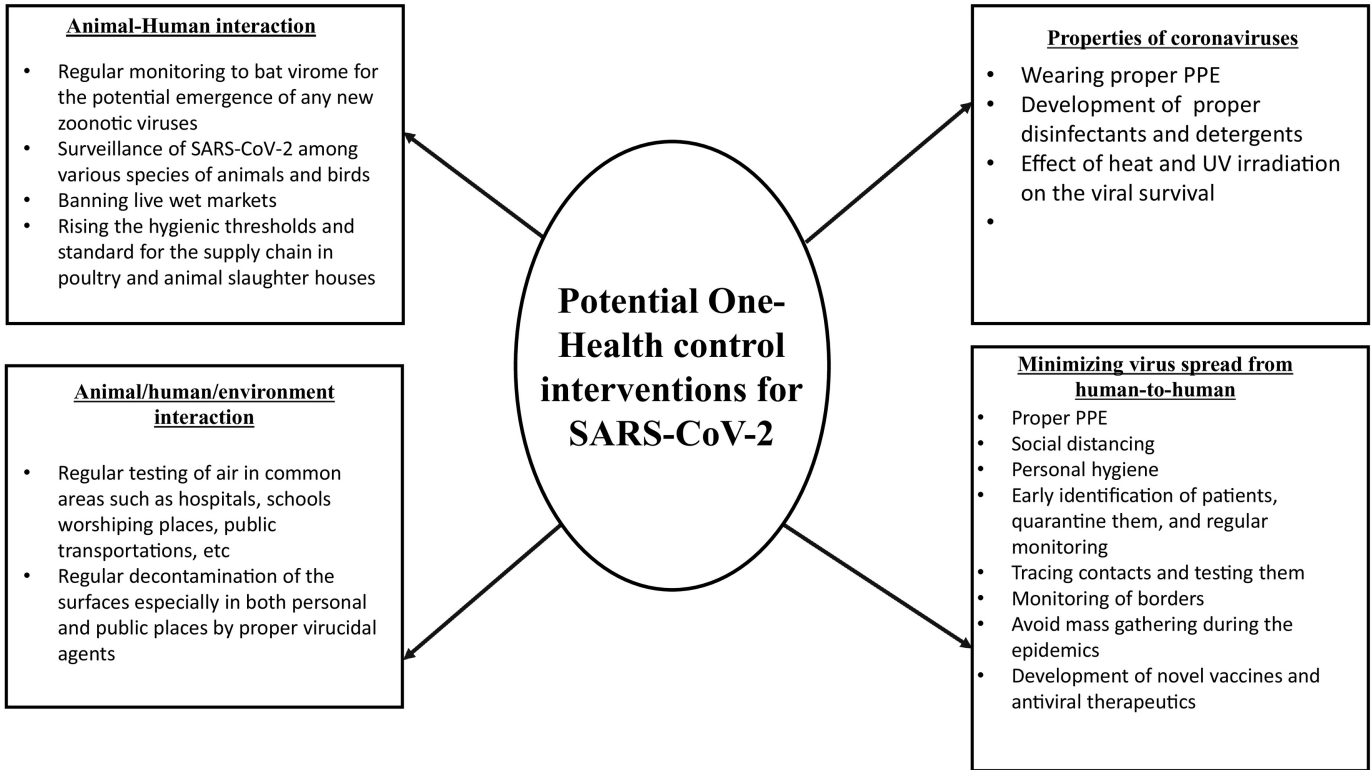


Figure 2