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Review Article

A Literature Review on the Epidemiology, Virology, Clinical Characteristics, Prevention and Treatment of Novel Coronavirus (2019-nCoV)

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Abstract

The World Health Organization (WHO) has issued a public health emergency of international concern for the outbreak of the novel coronavirus (2019-nCoV). This study aimed to review the findings of recent published literature to provide researchers with information regarding the current biggest global health threat of 2019-nCoV pandemic on the basis of previous coronaviruses. To do so, this study attempted to review the available online data on biological nature of 2019-nCoV compared to previous coronaviruses. Additionally, the epidemiology, susceptible population, transmission routes, clinical characteristics, and medications for 2019-nCoV were reviewed. In this article, after an introduction to the subject and characterization of coronavirus, we considered the experiences and lessons learned from previous outbreaks to review the epidemiology, clinical characteristics, prevention, and medications of 2019-nCov disease. There are three main routes for transmission of 2019-nCoV including close contact to infected cases, aerosol, and touch transmissions. This newfound virus can be transmitted from asymptomatic patients or from infected cases with symptoms ranging from a flu-like to severe respiratory syndrome. Currently, there are no 100% approved therapeutic drugs and vaccination for this disease. In conclusion, given that development of vaccine for 2019-nCoV requires close collaboration of vaccine manufacturers and biotechnology companies, which takes a long period for production of vaccine, implementation of prevention and controlling measures based on the current available information about the subject is the best measure to control the spread of the virus.

Keywords: 2019-nCoV, COVID-19, Pandemic, Epidemiology, Prevention, Clinical characteristics, Treatment, Coronavirus, Transmission routes, Outbreak

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Introduction

The super-spread of the novel coronavirus (2019-nCoV) not only has led to many deaths and disabilities, but also has brought social and economic downturns. On January 7, 2020, the World Health Organization (WHO) named the novel coronavirus as 2019-nCoV or officially as COVID-19 (1). The 2019-nCoV outbreak was characterized as a Public Health Emergency of International Concern (PHEIC) and a pandemic in January and March, 2020, respectively (2). The zoonotic coronaviruses of 2019-nCoV, SARS (severe acute respiratory syndrome), and MERS (Middle East respiratory syndrome) were originated in China in 2019, 2002, and 2012, respectively (3-5). The single-stranded RNA virus of 2019-nCoV belongs to subgenus *Sarbecovirus*, which is phylogenetically closest to the SARS-related coronaviruses first extracted from horseshoe bats in 2015-17 (6). At the outset of coronavirus outbreak, the disease was linked to Huanan seafood markets and consumption of slaughtered game meats (3). To terminate the animal to human transmission of the disease, regulatory measures on sale and consumption of game meats were taken. The Huanan seafood market was closed on January 1, 2020 (4). However, this virus showed further intercity spread after the control strategies to reduce the shedding from animal to human. The subsequent studies on rapid flourishing of disease indicated the transmission of 2019-nCoV between human populations other than animal-human transmission (5). The studies on family clusters reported person-to-person

transmission of 2019-nCoV (7). Therefore, practical implementation of control measures should be considered as a critical solution to the wide spread of this virus throughout different countries. The decision-makers consider the high costs of implementation of control measures rather than the benefits of prompt controls (8). Therefore, delay in taking prompt decisions such as travel restrictions and quarantining may cause the rapid spread of disease to other geographical regions. Other than wrong decisions, the delay in warning people might be due to consequences of causing fear (9). However, lack of transparency results in intimidation of clinician and allows the speculation and rumours regarding the spread of disease (10). Therefore, there is an urgent need in raising awareness on the biological nature, epidemiology, and clinical characteristics of 2019-nCoV to control the pandemic.

Methods

The English databases including Google Scholar, Scopus, ScienceDirect, Web of Science, and PubMed were searched using the following keywords: "COVID-19 pandemic", "epidemiology", "prevention", "clinical characteristics", "treatment", "coronavirus", and "transmission routes" .

This study aimed to review the findings of recent published literature to provide researchers with information regarding the current biggest global health threat of 2019-nCoV pandemic on the basis of previous coronaviruses. In this article, after an introduction to the subject and characterization of coronavirus, we consider the experiences and lessons learned from previous outbreaks to review the epidemiology, clinical characteristics, prevention, and medications of 2019-nCov disease.

Results

Characterization of 2019-nCoV

The 2019-nCoV contains a single stranded, non-segmented, positive sense RNA with 29.891 nucleotides which encodes 9860 amino acids (Figure 1) (11). The polyadenylated and encapsulated RNA of 2019-nCoV encodes different structural and non-structural genes (10-12). The nucleocapsid and spike proteins are responsible for RNA synthesis and viral entry, whereas membrane and envelope proteins are associated with viral assembly (8). The outer membrane of the enveloped 2019-nCoV is susceptible to oxidants including the chlorine in tap water. This virus is inactivated faster than non-enveloped viruses such as rotavirus or hepatitis A (8). The first step of infection by coronavirus occurs by attachment of spike protein to human cells. The ACE2 (angiotensin-converting enzyme 2) in the lower respiratory tract is known to be the receptor used for cell entry of both SARS and 2019-nCoV viruses (8, 13). The RNA genome encoding will take place after entering to human cells (14, 15). The pleomorphic RNA genome of 2019-nCov is known to be the largest genome among all RNA viruses (16, 17). The genome sequence of 2019-nCoV was recognised within few weeks in China which resulted in rapid development of diagnostic assays (18). The 2/3 of 2019-nCoV RNA encodes RdRp, ORF1a-ORF1b, and RNA synthesis materials and 1/3 of the rest encodes the four structural proteins of membrane, envelope, spike, and nucleocapsid (11, 19, 20). The initial studies indicated that bamboo rats, snakes, and raccoons are the main reservoirs of this virus (21), but further analysis showed that BatCoV RaTG13 and probably pangolin are the original sources (22, 23). The betacoronavirus of 2019-nCoV belongs to *Coronaviridae* subfamily of Coronaviridae family (22). 2019-nCoV causes serious problems of respiratory, hepatic, gastrointestinal, and neurologic systems in infected cases including SARS, metabolic acidosis, septic shock, dysfunctions, and may lead to death (16, 24, 25). Extreme precautions should be practiced by susceptible groups of elder and immunocompromised people suffering from chronic diseases including respiratory problems, diabetes, high blood pressure, and angiocardiopathy who experience severe symptoms of this disease (17, 25).

Comparison of 2019-nCoV, SARS and MERS Coronaviruses

All the three zoonotic viruses of 2019-nCoV, SARS, and MERS are originated from China in 2019, 2002, and 2012, respectively (26, 27). In 2003, the SARS outbreak resulted in more than 8000 infected cases and 800 (10%) deaths in 26 countries (28). Both 2019-nCoV and SARS viruses occurred during the traditional Spring Festival in which nearly 3 billion people travel countrywide (11). As reported from Chinese studies, 2019-nCoV, MERS and SARS mortality rates are 2.2, 35 and 10%, respectively (8). Figure has been calculated by 35% and 10% for MERS and SARS outbreaks, respectively, and for 2019-nCoV outbreak, the statistics for 16 April is reported. As shown in Figure 2, the overall mortality rate of 2019-nCoV is lower than SARS, but it has posed a severe threat to public health of all countries around the world (9). The literature shows a 2.2% mortality rate for 2019-nCoV outbreak, but the WHO situation report-87 (16 April, 2020) shows a 6.57% mortality rate for 2019-nCoV (Figure 2).

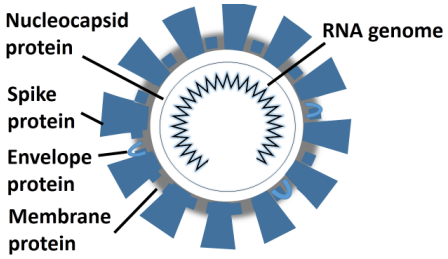

Figure 1. Structure of 2019-nCov; the RNA is surrounded by an envelope compromising of different proteins (25).

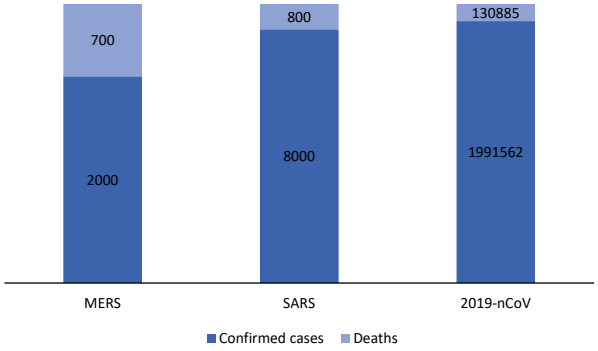

Figure 2. Comparison of Three Major Coronavirus Outbreaks by Number of Infected and Died Cases.

The symptoms of 2019-nCoV, SARS, and MERS coronaviruses ranges from a flu-like to severe respiratory syndrome (7, 29). The symptoms of fever, dry non-productive cough, and shortness of breath are same for both SARS and 2019-nCoV (16, 18). The diarrhoea occurs in 20%-25% of MERS and SARS cases, whereas gastrointestinal symptoms is rarely reported in 2019-nCoV infected cases (17). MERS infects cardiovascular system more than SARS and 2019-nCoV, which requires vasopressor treatment (12, 17, 30, 31). SARS, MERS, and 2019-nCoV involves young, aged above 50 years, and middle age and above groups of people, respectively (32). Unlike SARS, 2019-nCoV involves males more than females (8, 33). The incubation time for 2019-nCoV is approximately 5-6 days (34). The mean duration of infectiousness is almost similar to SARS (4.4-7.5 days) for serial interval (35). 2019-nCoV infectiousness begins before the onset of symptoms, whereas SARS has no pre-symptomatic infectiousness (8). The transmission can occur during asymptomatic incubation period (8). Only 6% of 2019-nCoV patients are critically ill and 14% of them show severe symptoms. Moreover, 80% of infected cases are asymptomatic or have mild disease (10). The therapeutic drugs for SARS were developed one year after its outbreak, whereas the effective drug of 2019-nCoV is still under clinical experimental phase (8). However, combination of lopinavir and ritonavir as an effective drug for SARS and MERS is also recommended for treatment of 2019-nCoV (36, 37).

Transmission Routes of 2019-nCoV

There exists a major gap in knowledge of epidemiology and clinical characteristics of this disease and many questions about its nature and transmission are unanswered. It is reported that 2019-nCov survives 2 hours in the air (17, 38, 39). Although the fecal-oral route of transmission was reported, the respiratory droplets (cough or sneeze) is currently known as the main transmission conduit of 2019-nCoV (25, 31). The RNA fragments of 2019-nCoV have been detected in faecal matter of infected cases and in one study the virus was cultured from a single stool specimen (17, 37, 40). Generally, there are three main routes for transmission of 2019-nCoV including close contact to infected cases, aerosol, and touch (41).

Epidemiology of 2019-nCoV Disease

The 27 cases of pneumonia with 7 severe infected cases on 31 December 2019 involved the world with an outbreak (42). With a ten-fold increase of confirmed cases from 23 to 30 January 2020, WHO called this outbreak a PHEIC on January 30, 2020 (8). The number of infected cases increased to three fold on February 6, 2020 (17). As reported by national authorities in WHO reports, on March 25, 2020, the global confirmed cases of 2019-nCoV were 414 179, with 18 440 deaths. However, the number of infected cases increased by time. On April 16, 2020 (WHO, situation report-87), the confirmed cases (deaths in parenthesis) in western pacific, European, south-east Asia, eastern Mediterranean, Americas and African regions were 125 571 (4239), 1 013 093 (89 317), 21 790 (990), 111 432 (5532), 707 121 (302 450), and 11 843 (550), respectively (43). According to situation reports of WHO for 2019-nCoV, Figures 3 and 4 show the increase in total number of cases until date and also the new cases. The data on number of new infected and died cases was not reported on March 22, 2020 by WHO.

The number of cases by regions on April 16, 2020 is reported in Table 1 (43). According to the WHO, up to this date, the highest morbidity rate of COVID-19 belongs to the United States and the highest mortality rate of COVID-19 is in Italy (43).

Clinical Characteristics of 2019-nCoV

Fever of (≥38.0°C), shortness of breath or dyspnea, and non-productive dry cough are the three most common symptoms of 2019-nCoV disease. Other symptoms include sore throat, fatigue, headache, myalgia, diarrhoea, vomiting, and chills (10, 18, 42). Severe infection leads to acute kidney injury and features of acute respiratory distress syndrome, metabolic acidosis, septic shock, and dysfunctions (10, 42, 44). These symptoms can lead to the death of infected cases. Confirmation of infection can be conducted by genome sequencing and phylogenetic analysis of bronchoalveolar lavage fluid of suspected cases (45). The two molecular methods of real-time polymerase chain reaction (RT-PCR) and Reverse Transcription are the most common methods to diagnosis the virus. The RNA is extracted from bronchoalveolar lavage fluid and oropharyngeal swabs, deep tracheal aspirate, and sputum as respiratory samples. The lower respiratory samples are prior to the upper one due to higher viral content (46). The RT-PCR method is highly specific and quantifies the target genome by florescence data. This method is useful for identification of infection in both suspected and infected cases. The sensitivity of molecular methods is higher than antibody detection and are much more suitable for diagnostic tests and epidemiological reports

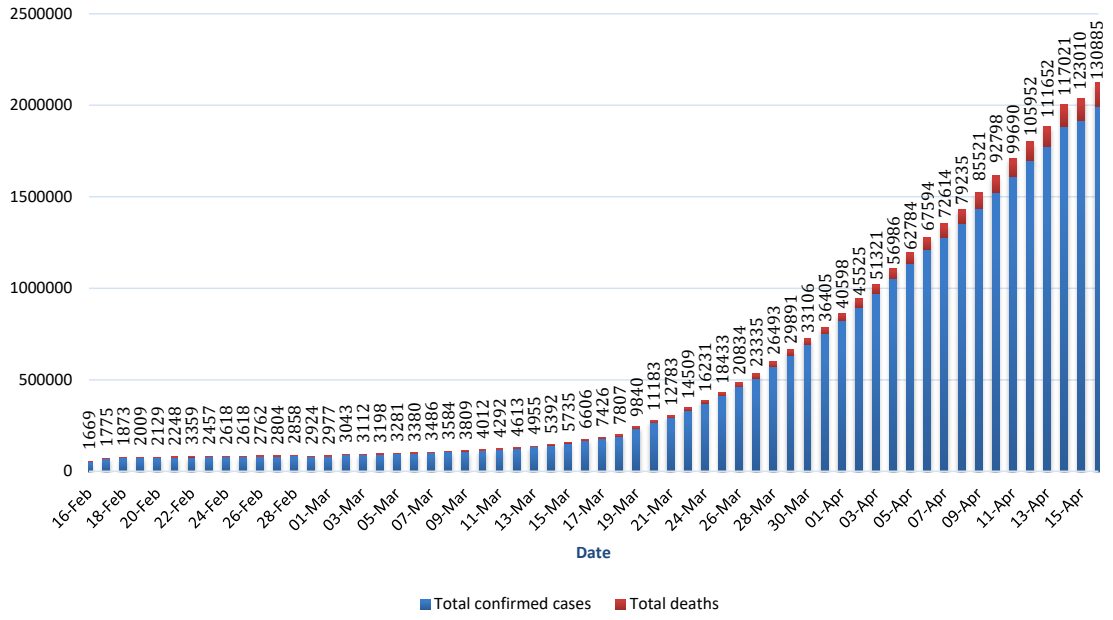

Figure 3. The Total Number of 2019-nCoV Infected and Died Cases (WHO Situation Reports 27-87) (29). The data label inside each column shows the number of total deaths (red color).

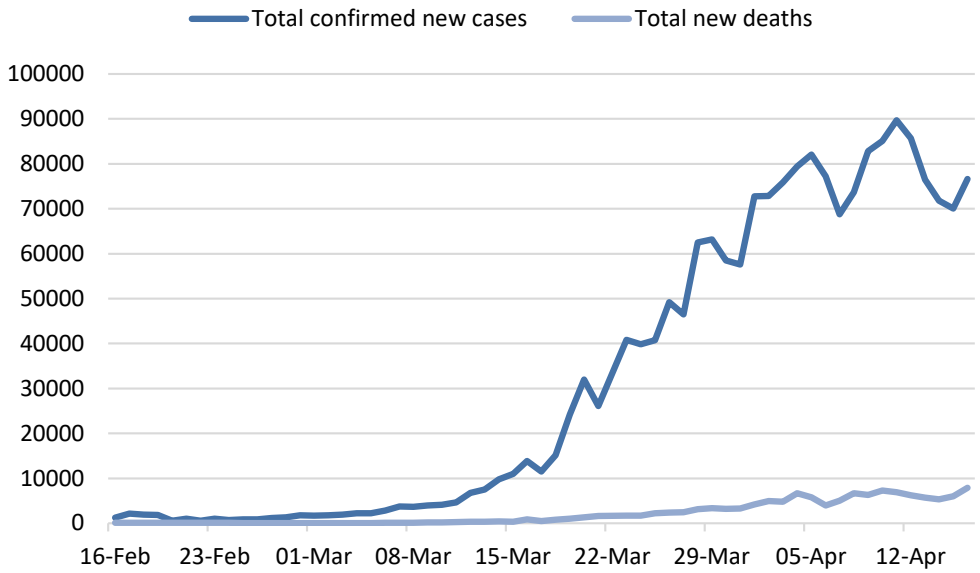

Figure 4. Comparison of Total Number of New Confirmed and Died Cases (WHO Situation Reports 27-87) (29). The data label inside each column shows the number of total deaths (red color).

Table 1. The Number of Cases and Deaths of COVID-19 Pandemic on 16 April 2020

Region	The Highest Morbidity	The Highest Mortality	Number of Countries Affected by the COVID-19 Pandemic
Western Pacific Region	China (83 797)	China (3352)	15
European Region	Spain (177 633)	Italy (21 647)	53
South-East Asia Region	India (123 80)	Indonesia (469)	10
Eastern Mediterranean Region	Iran (76 389)	Iran (4777)	21
Region of the Americas	United States of America (604 070)	United States of America (25 871)	35
African region	South Africa (2506)	Algeria (336)	45

(22). The 2019-nCoV test kits were first available on January 13, 2020 (22). The RT-PCR is advantageous over other methods and several samples can be processed in one run simultaneously. Infected cases may have higher rate of erythrocyte sedimentation and elevated contents of lactate dehydrogenase, C-reactive, and creatinine proteins (47).

Almost all the cases suffer from pneumonia, thereby, asymptomatic and suspected cases can be examined by computerized tomography (CT) scan of their chest exhibiting ground glass opacity and bilateral patchy shadowing appearance (22, 46). Figure 5 shows the axial CT scan of lung in 2019-nCoV infected cases.

In an American study on tested individuals in January 2020 (N = 210, 6: airport screening, 178: health care setting, and 26: contact tracing). Furthermore, 138 and 115 cases were in age range of 18-49 years and male sex groups, respectively. Moreover, 42, 4, and 1 individuals were hospitalized, admitted to intensive care unit, and died, respectively. From 210 tested individuals, 148 were travellers from china and the rest were in close contact to infected cases (22). In a Chinese report the male:female ratio for 2019-nCoV was 1.39:1, which was comparable to a ratio from an American report (48).

Prevention and Treatment of 2019-nCoV

Currently, there is no fully-approved vaccine or an effective therapeutic drug for 2019-nCoV disease. In a study by Sanami et al, a multiepitope COVID-19 vaccine was designed using an immunoinformatic approach. In this study, the binding affinity and stability of vaccine were evaluated by molecular docking and molecular dynamics, respectively. In addition, the expression level of this vaccine was evaluated in *Escherichia coli* (49).

Therefore, implementation of prevention and control measures is the most crucial means to curb the outbreak. The prevention and control measures associated with containment of current 2019-nCoV outbreak are personal controlling behaviors such as hand hygiene, self-isolation, mask wearing, social distancing, and disinfection of contact surfaces and social controlling behaviors such as isolation, quarantine, and raising of public awareness (50). For example, hand hygiene is the most efficient and easiest method to prevent the infectious diseases. The adherence to hand hygiene is associated with the awareness on its benefits and the available facilities. The proper hand washing practices should be educated to prevent the transmission of 2019-nCoV. Those who had experienced the education for hand hygiene in other outbreaks are much more aware from hand washing practices than others (51). The hand washing behavior might be related to different factors such as gender, incomes, etc. For example, men and low-income individuals wash their hands less frequently than women and high-income individuals (51). This method is simple and cost-effective. A study in Nigeria showed that 72.4% of 116 health care workers were well aware of proper hand washing techniques (52). Another efficient and easy personal preventive behavior is wearing mask. As studies show, wearing masks significantly reduces the spread of virus (53, 54), and it can reduce the shedding of virus aerosols up to 3.4 fold. The RNA of flu virus in fine and coarse aerosol fraction decreases to 25 and 2.8 fold in the number of viral copies, respectively (55). A random trial showed that the correct use of masks can help reduce the likelihood of developing transmission to health care workers (56).

Currently, there are no specific effective therapeutic drugs for 2019-nCoV. Paracetamol and expectorants may be prescribed for fever and cough, respectively (57). The severe respiratory syndrome and distress or shock require immediate oxygen therapy (22). Interferon alpha and a combination of lopinavir and ritonavir as an effective drug for SARS and MERS are also recommended for medication of 2019-nCoV virus (48). For the infected cities which are under lockdown, the medicinal materials should be carefully provided to reduce the mortality rate and improve cure rates (22). In SARS outbreak,

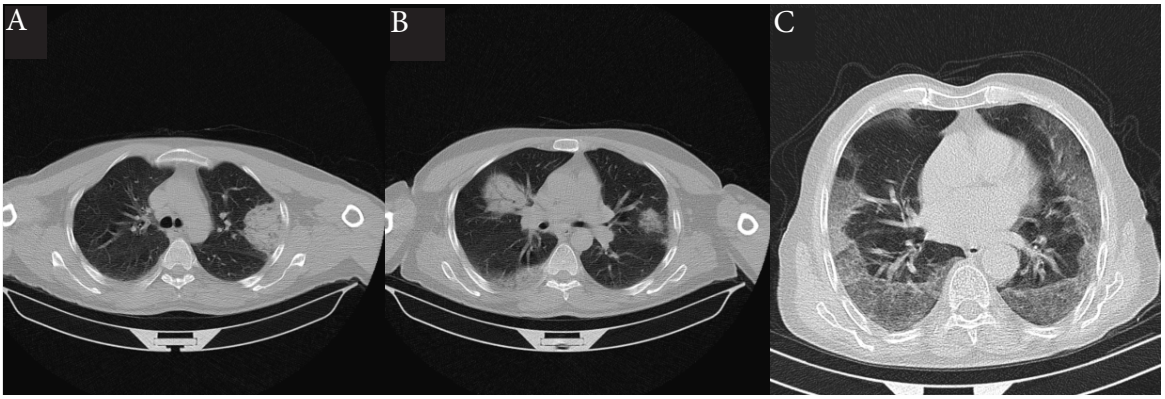

Figure 5. Axial Computerized Tomography of Lungs in 2019-nCoV Infected Cases. A: CT image of patient with fever, cough, and positive RT-PCR test that shows a peripheral consolidation, B: CT image of patient with fever, cough, and positive RT-PCR test that shows multiple subpleural, peribronchovascular consolidation and ground glass opacities and, C: CT image of patient with fever, respiratory distress, and positive RT-PCR test that shows bilateral peripheral ground glass opacities.

there were many obstacles regarding the development of vaccine, including lack of comprehensive information on nature and mechanism of pathogen, necessity of testing the efficacy in involved areas, incompatibility to human models, etc (22).

Conclusion

There is a major gap in knowledge of epidemiology and clinical characteristics of this disease and many questions about its nature and transmission are unanswered. Understanding the virus and its epidemiology and clinical characteristics have an important role in spread and control of this disease. Implementation of personal and social prevention behaviors such as quarantine, early diagnosis and isolation of suspected/infected cases, personal hygiene practices, timely dissemination of clear and accurate information, and social distancing are of the most effective prevention methods which can suppress the peak and slowdown the high spread of 2019-nCov until therapeutic drugs and vaccines be produced.

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Author's Contribution

VR and ZP wrote the manuscript. LH, ZP, and AHM collected the data, revised the literature, and contributed to conception and design of the study. All authors contributed to critical revision, edition, and final approval of the manuscript.

Conflict of Interest Disclosure

The authors declare that they have no conflict of interests.

Ethical Statement

Not applicable.

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Informed Consent

Not applicable.

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