Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19)

16-24 February 2020

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I. The Mission

Goal and Objectives

The overall goal of the Joint Mission was to rapidly inform national (China) and international planning on next steps in the response to the ongoing outbreak of the novel coronavirus disease (COVID-19¹) and on next steps in readiness and preparedness for geographic areas not yet affected.

The major objectives of the Joint Mission were as follows:

- To enhance understanding of the evolving COVID-19 outbreak in China and the nature and impact of ongoing containment measures;
- To share knowledge on COVID-19 response and preparedness measures being implemented in countries affected by or at risk of importations of COVID-19;
- To generate recommendations for adjusting COVID-19 containment and response measures in China and internationally; and
- To establish priorities for a collaborative programme of work, research and development to address critical gaps in knowledge and response and readiness tools and activities.

Members & Method of Work

The Joint Mission consisted of 25 national and international experts from China, Germany, Japan, Korea, Nigeria, Russia, Singapore, the United States of America and the World Health Organization (WHO). The Joint Mission was headed by Dr Bruce Aylward of WHO and Dr Wannian Liang of the People's Republic of China. The full list of members and their affiliations is available in Annex A. The Joint Mission was implemented over a 9-day period from 16-24 February 2020. The schedule of work is available in Annex B.

The Joint Mission began with a detailed workshop with representatives of all of the principal ministries that are leading and/or contributing to the response in China through the National Prevention and Control Task Force. A series of in-depth meetings were then conducted with national level institutions responsible for the management, implementation and evaluation of the response, particularly the National Health Commission and the China Centers for Disease Control and Prevention (China CDC). To gain first-hand knowledge on the field level implementation and impact of the national and local response strategy, under a range of epidemiologic and provincial contexts, visits were conducted to Beijing Municipality and the provinces of Sichuan (Chengdu), Guangdong (Guangzhou, Shenzhen) and Hubei (Wuhan). The field visits included community centers and health clinics, country/district hospitals, COVID-19 designated hospitals, transportations hubs (air, rail, road), a wet market, pharmaceutical and personal protective equipment (PPE) stocks warehouses, research institutions, provincial health commissions, and local Centers for

¹ In the Chinese version of this report, COVID-19 is referred to throughout as novel coronavirus pneumonia or NCP, the term by which COVID-19 is most widely known in the People's Republic of China.

Disease Control (provincial and prefecture). During these visits, the team had detailed discussion and consultations with Provincial Governors, municipal Mayors, their emergency operations teams, senior scientists, frontline clinical, public health and community workers, and community neighbourhood administrators. The Joint Mission concluded with working sessions to consolidate findings, generate conclusions and propose suggested actions.

To achieve its goal, the Joint Mission gave particular focus to addressing key questions related to the natural history and severity of COVID-19, the transmission dynamics of the COVID-19 virus in different settings, and the impact of ongoing response measures in areas of high (community level), moderate (clusters) and low (sporadic cases or no cases) transmission.

The findings in this report are based on the Joint Mission's review of national and local governmental reports, discussions on control and prevention measures with national and local experts and response teams, and observations made and insights gained during site visits. The figures have been produced using information and data collected during site visits and with the agreement of the relevant groups. References are available for any information in this report that has already been published in journals.

The final report of the Joint Mission was submitted on 28 February and updated 11 March.

II. Major findings

The major findings are described in six sections: the virus, the outbreak, transmission dynamics, disease progression and severity, the China response and knowledge gaps. More detailed descriptions of technical findings are provided in Annex C.

The virus

On 30 December 2019, three bronchoalveolar lavage samples were collected from a patient with pneumonia of unknown etiology – a surveillance definition established following the SARS outbreak of 2002-2003 – in Wuhan Jinyintan Hospital. Real-time PCR (RT-PCR) assays on these samples were positive for pan-Betacoronavirus. Using Illumina and nanopore sequencing, the whole genome sequences of the virus were acquired. Bioinformatic analyses indicated that the virus had features typical of the coronavirus family and belonged to the Betacoronavirus 2B lineage. Alignment of the full-length genome sequence of the COVID-19 virus and other available genomes of Betacoronavirus showed the closest relationship was with the bat SARS-like coronavirus strain BatCov RaTG13, identity 96%.

Virus isolation was conducted with various cell lines, such as human airway epithelial cells, Vero E6, and Huh-7. Cytopathic effects (CPE) were observed 96 hours after inoculation. Typical crown-like particles were observed under transmission electron microscope (TEM) with negative staining. The cellular infectivity of the isolated viruses could be completely neutralized by the sera collected from convalescent patients. Transgenic human ACE2 mice and Rhesus monkey intranasally challenged by this virus isolate induced multifocal pneumonia with interstitial hyperplasia. The COVID-19 virus was subsequently detected and isolated in the lung and intestinal tissues of the challenged animals. Whole genome sequencing analysis of 104 strains of the COVID-19 virus isolated from patients in different localities with symptom onset between the end of December 2019 and mid-February 2020 showed 99.9% homology, without significant mutation (Figure 1).



Figure 1. Phylogenetic analysis of the COVID-19 virus and its closely related reference genomes

Note: COVID-19 virus is referred to as 2019-nCoV in the figure, the interim virus name WHO announced early in the outbreak.

Post-mortem samples from a 50-year old male patient from Wuhan were taken from the lung, liver, and heart. Histological examination showed bilateral diffuse alveolar damage with cellular fibromyxoid exudates. The lung showed evident desquamation of pneumocytes and hyaline membrane formation, indicating acute respiratory distress syndrome (ARDS). Lung tissue also displayed cellular and fibromyxoid exudation, desquamation of pneumocytes and pulmonary oedema. Interstitial mononuclear inflammatory infiltrates, dominated by lymphocytes, were seen in both lungs. Multinucleated syncytial cells with atypical enlarged pneumocytes characterized by large nuclei, amphophilic granular cytoplasm, and prominent nucleoli were identified in the intra-alveolar spaces, showing viral cytopathic-like changes. No obvious intranuclear or intracytoplasmic viral inclusions were identified.

The outbreak

As of 20 February 2020, a cumulative total of 75,465 COVID-19 cases were reported in China. Reported cases are based on the National Reporting System (NRS) between the

National and Provincial Health Commissions. The NRS issues daily reports of newly recorded confirmed cases, deaths, suspected cases, and contacts. A daily report is provided by each province at 0300hr in which they report cases from the previous day.

The epidemic curves presented in Figures 2 and 3 are generated using China's National Infectious Disease Information System (IDIS), which requires each COVID-19 case to be reported electronically by the responsible doctor as soon as a case has been diagnosed. It includes cases that are reported as asymptomatic and data are updated in real time. Individual case reporting forms are downloaded after 2400hr daily. Epidemiologic curves for Wuhan, Hubei (outside of Wuhan), China (outside Hubei) and China by symptom onset are provided in Figure 2.



Figure 2 Epidemiologic curve of COVID-19 laboratory confirmed cases, by date of onset of illness, reported in China, as of 20 February 2020

Figure 3 presents epidemic curves of laboratory-confirmed cases, by symptom onset and separately by date of report, at 5, 12, and 20 February 2020. Figures 2 and 3 illustrate that the epidemic rapidly grew from 10-22 January, reported cases peaked and plateaued between 23 January and 27 January, and have been steadily declining since then, apart from the spike that was reported on 1 February (note: at a major hospital in Wuhan, fever clinic patients fell from a peak of 500/day in late January to average 50/day since mid-February).



Figure 3. Epidemic curves by symptom onset and date of report as of 5 February (top panel), 12 February (middle panel) and 20 February 2020 (lower panel) for laboratory confirmed COVID-19 cases for all of China

Based on these epidemic curves, the published literature, and our on-site visits in Wuhan (Hubei), Guangdong (Shenzhen and Guangzhou), Sichuan (Chengdu), and Beijing, the Joint Mission team has made the following epidemiological observations:

Demographic characteristics

Among 55,924 laboratory confirmed cases reported as of 20 February 2020, the median age is 51 years (range 2 days-100 years old; IQR 39-63 years old) with the majority of cases (77.8%) aged between 30–69 years. Among reported cases, 51.1% are male, 77.0% are from Hubei and 21.6% are farmers or laborers by occupation.

Zoonotic origins

COVID-19 is a zoonotic virus. From phylogenetics analyses undertaken with available full genome sequences, bats appear to be the reservoir of COVID-19 virus, but the intermediate host(s) has not yet been identified. However, three important areas of work are already underway in China to inform our understanding of the zoonotic origin of this outbreak. These include early investigations of cases with symptom onset in Wuhan throughout December 2019, environmental sampling from the Huanan Wholesale Seafood Market and other area markets, and the collection of detailed records on the source and type of wildlife species sold at the Huanan market and the destination of those animals after the market was closed.

Routes of transmission

COVID-19 is transmitted via droplets and fomites during close unprotected contact between an infector and infectee. Airborne spread has not been reported for COVID-19 and it is not believed to be a major driver of transmission based on available evidence; however, it can be envisaged if certain aerosol-generating procedures are conducted in health care facilities. Fecal shedding has been demonstrated from some patients, and viable virus has been identified in a limited number of case reports. However, the fecal-oral route does not appear to be a driver of COVID-19 transmission; its role and significance for COVID-19 remains to be determined. Viral shedding is discussed in the Technical Findings (Annex C).

Household transmission

In China, human-to-human transmission of the COVID-19 virus is largely occurring in families. The Joint Mission received detailed information from the investigation of clusters and some household transmission studies, which are ongoing in a number of Provinces. Among 344 clusters involving 1308 cases (out of a total 1836 cases reported) in Guangdong Province and Sichuan Province, most clusters (78%-85%) have occurred in families. Household transmission studies are currently underway, but preliminary studies ongoing in

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