Research Assessment Exercise 2020
Impact Case Study

University: The University of Hong Kong (HKU)
Unit of Assessment (UoA): 03 - Clinical Medicine
Title of case study: Transforming local and global responses to emerging infectious diseases

(1) Summary of the impact

Researchers at the University of Hong Kong (HKU) have developed and applied multiple evidenced-based approaches to control emerging influenza viruses and coronaviruses in animals and humans in Asian, Middle East and African countries. These approaches include providing diagnostic tests, trainings, risk assessment tools, vaccine strains candidates and surveillance protocols. The team has developed guidelines and action plans which have been implemented by governmental and healthcare organisations at local, regional and global levels to control these pathogens. We have also collaborated with companies to develop diagnostic (e.g. H7N9 Influenza Rapid Detection Test, Arbor Vita) and medical products (Experimental influenza vaccine, InvVax) that are relevant to these diseases.

(2) Underpinning research

Key HKU School of Public Health Researchers:
Professor Gabriel Leung, Dean of Medicine (1999-now)
Professor Malik Peiris (1995-now)
Professor Yi Guan (2000-now)
Professor Leo Poon (2001-now)
Professor Ben Cowling (2004-now)

Following the outbreak of highly pathogenic avian influenza A H5N1, the HKU team played a critical role in public health response, continued to report on the re-emergence of the H5N1 virus in 2000 and beyond. We reported the continued genetic changes of the H5N1 virus, its re-adaptation to chicken, its re-emergence in live poultry markets and farms in Hong Kong. We documented the key role of live poultry markets in the amplification and persistence of these viruses, and in the dissemination of these viruses back to poultry farms in 2004 (3.1). We also reported the evolution relationship of H5N1 viruses found in China, Southeast Asia, Europe, Africa and Middle East.

In 2003, Hong Kong was at the epicentre of the Severe Acute Respiratory Syndrome (SARS) outbreak. We were the first to identify that SARS was caused by a novel coronavirus (3.2), developed and implemented diagnostics serving the whole of Hong Kong and beyond, demonstrated that the virus was shed in the faeces as well as the respiratory secretions (information crucial to understand the Amoy Gardens outbreak), implemented case-control studies to identify effective control measures, demonstrated the low viral load in first 5 days of illness (implying lower transmission early in illness), and showed that asymptomatic infection was uncommon – these factors together explaining the feasibility and effectiveness of public health interventions in stopping the outbreak. We showed the role of live game animal markets in Guangdong as sources of this zoonotic agent in 2003 (3.3), and provided evidence to shut down these markets thereby preventing a possible re-emergence of SARS.

In 2009, we demonstrated the underlying mechanisms of the emergence of the 2009 pandemic virus and contributed to defining some of the viral genetic mechanisms underlying its emergence. By 2010, ~50% of all swine influenza virus sequences in the global data bases that were crucial to understand pandemic emergence came from the HKU group (3.4). Based on the infrastructure for community-based studies that we had established, we were able to provide some of the earliest estimates of transmissibility and clinical severity of the new 2009 pandemic virus (3.5).

We identified the mechanisms accounted for the genesis of human H7N9 virus in 2012. Our work demonstrated that the poultry industry and marketing system in Mainland China allow frequency

reassortment of viruses from terrestrial and aquatic poultry (3.6). This implies that the separation of the marketing chains of terrestrial and aquatic poultry is a generic intervention to minimize emergence of such viruses in future. Through phylogenetic studies we demonstrated the dissemination of and establishment of H7N9 lineages in different regions of China. We performed a comprehensive risk assessment, including the characteristics of the virus, the characteristics of the cases, the predominance of recent live poultry exposures among cases, the incubation period, the fatality risks of symptomatic cases and hospitalised cases, and the impact of live poultry market closures.

(3) References to the research

3.1 Li KS, Guan Y, Wang J, Smith GJ, Xu KM, Duan L, Rahardjo AP, Puthavathana P, Buranathai C, Nguyen TD, Estoepangestie AT, Chaisingh A, Auewarakul P, Long HT, Hanh NT, Webby RJ, Poon LL, Chen H, Shortridge KF, Yuen KY, Webster RG, Peiris JS. Genesis of a highly pathogenic and potentially pandemic H5N1 influenza virus in eastern Asia. Nature. 2004 Jul 8;430(6996):209-13. DOI: 10.1038/nature02746

3.2 Peiris JSM, Lai ST, Poon LL, Guan Y, Yam LY, Lim W, Nicholls J, Yee WK, Yan WW, Cheung MT, Cheng VC, Chan KH, Tsang DN, Yung RW, Ng TK, Yuen KY; SARS study group. Coronavirus as a possible cause of severe acute respiratory syndrome. Lancet. 2003 Apr 19; 361(9366):1319-25. DOI: 10.1016/s0140-6736(03)13077-2

3.3 Guan Y, Zheng BJ, He YQ, Liu XL, Zhuang ZX, Cheung CL, Luo SW, Li PH, Zhang LJ, Guan YJ, Butt KM, Wong KL, Chan KW, Lim W, Shortridge KF, Yuen KY, Peiris JS, Poon LL. Isolation and characterization of viruses related to the SARS coronavirus from animals in southern China. Science. 2003 Oct 10;302(5643):276-8. DOI: 10.1126/science.1087139

3.4 Vijaykrishna D, Smith GJ, Pybus OG, Zhu H, Bhatt S, Poon LL, Riley S, Bahl J, Ma SK, Cheung CL, Perera RA, Chen H, Shortridge KF, Webby RJ, Webster RG, Guan Y, Peiris JS. Long-term evolution and transmission dynamics of swine influenza A virus. Nature. 2011 May 26;473(7348):519-22. DOI: 10.1038/nature10004

3.5 Cowling BJ, Chan KH, Fang VJ, Lau LLH, So HC, Fung ROP, Ma ESK, Kwong ASK, Chan CW, Tsui WWS, Ngai HY, Chu DWS, Lee PWY, Chiu MC, Leung GM, Peiris JSM. Comparative epidemiology of pandemic and seasonal influenza A in households. N Engl J Med. 2010 Jun 10;362(23):2175-84. DOI: 10.1056/NEJMoa0911530

3.6 Zhu H, D Wang, Kelvin DJ, Li L, Zheng Z, Yoon SW, Wong SS, Farooqui A, Wang J, Banner D, Chen R, Zheng R, Zhou J, Zhang Y, Hong W, Dong W, Cai Q, Roehr MHA, Huang SSH, Kelvin AA, Yao T, Zhou B, Chen X, Leung GM, Poon LLM, Webster RG, Webby RJ, Peiris JSM, Guan Y, Shu Y. Infectivity, transmission, and pathology of human-isolated H7N9 influenza virus in ferrets and pigs. Science. 2013 Jul 12;341(6142):183-6. DOI: 10.1126/science.1239844

Key research program grants:

- PI: Peiris JSM. Control of Pandemic and Inter-Pandemic Influenza (HK University Grants Committee Areas of Excellence Scheme, 2008-16, HK$76M)
- PI: Peiris JSM. Viral, Host and Environmental Determinants of Influenza Virus Transmission and Pathogenesis (HK University Grants Committee Theme-based Research Scheme, 2015-20, HK$75M).

(4) Details of the impact

Impacts include: health and welfare, public policy and services, international development

Main Beneficiaries include: Governments (e.g. Hong Kong), World Health Organisation (WHO), Food and Agriculture Organisation (FAO) and World Organisation for Animal Health (OIE)

Our work have had direct impacts on the worldwide control of these pathogens:

Control of animal influenza viruses:

Our long-term influenza virus work (3.1) yielded evidence-based measures for controlling animal influenza, leading to reducing the risk of zoonotic transmission of influenza from animal to human. Some of these control strategies (e.g. market rest-day policy) are now being implemented elsewhere including in mainland China and beyond. For example, we are now contracted to conduct animal influenza surveillance for Hong Kong Government and our recommendations on Hong Kong Government's influenza vaccination policy on poultry ([Ai-ii], 2016).

Our real-time long-term monitoring of animal influenza activities (3.1, 3.4, 3.6) in local food chains and wildlife allowed us to provide early warnings to the Hong Kong Government about the potential health risk. These data allowed local authorities to implement prompt control measures (e.g. suspension of poultry trading; [B], 2016)

With our impacts on avian influenza control, HKU has been designated as a WHO H5 reference laboratory. HKU is heavily involved in various WHO activities and programs for influenza pandemic preparedness. The HKU team is one of the eight research groups globally to be consistently invited to the twice yearly WHO influenza vaccine strain selection. Eight H5N1 and 1 H5N6 WHO vaccine candidate strains arose from HKU. This team also assisted WHO to make standardized protocols to its member countries (>190) for influenza diagnosis ([Ci-iii], 2016).

HKU team members were involved in the development and implementation of the WHO "Tool for Influenza Pandemic Risk Assessment" (TIPRA), a systematic approach used by experts from WHO, OIE and FAO to risk assessing animal viruses for pandemic threat. This tool has been used by WHO for assessing the risk of 5 animal viruses (H1N1, H5N1, H5N6, H7N9, and H9N2)([Di-ii], 2016).

This team worked with more than 15 of companies that help to enhance the control of influenza virus. HKU members were involved in the characterization of broadly protective antibodies against influenza viruses (e.g. Crucell). HKU members evaluated an antigen test for H7N9 virus and, with the data generated from this team, this antigen test was approved by FDA (USA) in 2014 for diagnostic purpose ([E] for a FDA-approved product from Arbor Vita).

Control of influenza virus and other respiratory viruses in humans:

This team conducted several important epidemiological studies in human for SARS and pandemic H1N1 (3.2, 3.3, 3.5). Since 2014 the HKU has been designated as a WHO Collaborating Centre (WHOCC) for Infectious Disease Epidemiology and Control. This WHOCC coordinates research on the control and prevention of infectious diseases and providing local and regional education and training in infectious disease epidemiology and control. We have taught 6 short courses in infectious disease epidemiology and modelling in the past 5 years, in Hong Kong and in the region ([F], 2014). HKU members serve on key committees pertaining to emerging viral infections, including WHO and International Society for Influenza and other Respiratory Viruses, and hosts the secretariat for the Consortium for the Standardisation of Influenza Sero-epidemiology (CONSISE). Work from these organisations created new guidelines/standards to achieve better virus or serological surveillances, aiming for establishing more effective control measures for these infections. An example of pandemic preparedness plan contributed by a HKU member is shown ([G], 2017).

Control of emerging coronaviruses:

With their work generated from the SARS outbreak in 2003 (3.2, 3.3), HKU developed extensive research programs on emerging coronaviruses in humans and animals. These studied revealed major findings about the ecology, transmission and control measures of these novel coronaviruses. Because of these impacts, HKU has been well recognized as a major research hub for animal coronaviruses. HKU members have been invited to serve as advisors/experts in WHO to better control MERS in humans. They joined WHO missions to make new guidelines/recommendations to control MERS in humans (e.g. Republic of Korea in 2015 and Kingdom of Saudi Arabia in 2016) ([H] and [I], 2015) and provided training to healthcare workers in the affected region on laboratory diagnosis (e.g. United Arab Emirates in 2015) ([H] and [I], 2015).

HKU is actively involved in the control coronaviruses in animals (3.3). The HKU team contributed in understanding MERS-CoV in animals countries. These findings have major health implications.

Because of this, HKU has regularly sent its experts to serve in FAO and OIE to make guidelines/recommendation on farming, trading and veterinary practices (e.g. FAO mission in Saudi Arabia in 2013, FAO mission in United Arab Emirates in 2014, OIE ad hoc expert group on MERS in 2014). A report issued by OIE to its member countries (>180) is shown as an example ([Ji], 2014). This team also played a leading role in a FAO regional technical consultation meeting for MERS-CoV (Oman, 2014). In this meeting, representatives for 11 member countries (Bahrain, Egypt, Ethiopia, Jordan, Kuwait, Oman, Palestine, Qatar, Saudi Arabia, Sudan, United Arab Emirates, and Yemen) in the MERS-affected region agreed on several necessary actions for controlling MERS (Muscat declaration, 2014; [Jii]). In brief, these actions include: i) enhance surveillance, ii) develop policy to reduce transmission, iii) promote research, iv) promote data exchange and regional coordination and v) engaged stakeholders at different levels (e.g. veterinary officers, animal health experts, public health officials and administrators).

(5) Sources to corroborate the impact

[A] HKU's work informed government policy

i) A service contract to conduct avian influenza surveillance for Hong Kong Government (2018)

ii) News cutting: Hong Kong chickens could be given extra shot against H7 bird flu virus (2016)

[B] Long-term monitoring of animal influenza viruses activities in local food chains. Detection of H5N1 or H7N9 viruses in poultry by HKU would trigger governmental public health actions to control avian influenza viruses in poultry, such as suspension of live poultry trading and enhanced surveillance in poultry (A news cutting from 2016 as an example: Faecal droppings of live poultry from Yan Oi Market in Tuen Mun tested positive of H7N9 virus)

[C] HKU WHO H5 Reference Lab (2004-now)

i) Terms of reference

ii) Providing H5 strains as vaccine candidates (Example from 2016, page 7)

iii) Development of molecular diagnostic tests for WHO (Example from 2014; page 17)

[D] Influenza Pandemic Risk Assessment

i) WHO Tool for Influenza Pandemic Risk Assessment (2016; page 17)

ii) Animal influenza viruses assessed by WHO using TIPRA (2017; page 475)

[E] FDA approved diagnostic test for H7N9 detection (2014; page 15).

[F] WHO Collaborating Centre for Infectious Disease Epidemiology and Control (2014-now)

[G] A WHO Pandemic Influenza Risk Management (2017; page 6).

[H] WHO "International Health Regulations (2005) Emergency Committee concerning Middle East respiratory syndrome coronavirus (MERS-CoV)". HKU membership (2015-now)

[I] WHO Mission to Korea for a MERS outbreak in human (2015, page 13)

[J] Control of MERS-CoV in animals

i) OIE guidelines for MERS (2014); Section 2 on page 1. In this report, we shared epidemiological and diagnostic findings generated from HKU surveillance studies. This resulted in making bullet points 1, 2, 4, 6 and 12 in Section 5, pages 3-4; Term of reference of this ad-hoc group on page 6.

ii) Muscat declaration for controlling MERS-CoV in animals (2014; page 2)