Scientific Committee on Emerging and Zoonotic Disease and Scientific Committee on Vaccine Preventable Diseases

Consensus Interim Recommendations on the Use of COVID-19 Vaccines in Hong Kong

(As of Jan 7, 2021)

Introduction

The ongoing COVID-19 pandemic causes a significant disease burden worldwide. In Hong Kong, cases and outbreaks continue to be reported. To reduce the impacts of COVID-19 on health and society, vaccines against COVID-19 is considered an important public health tool for containing the pandemic in the medium and long term. On 7 January 2021, the Scientific Committee on Emerging and Zoonotic Diseases (SCEZD), the Scientific Committee on Vaccine Preventable Diseases (SCVPD), and the Expert Advisory Panel to Chief Executive (EAP) reviewed the latest scientific evidence on the epidemiology and clinical features of COVID-19, published data on the COVID-19 vaccines be procured by the Hong Kong SAR Government, local data as well as overseas recommendations/practices, and provides recommendations on the population groups and circumstances for the use of COVID-19 vaccines in Hong Kong.

COVID-19 Vaccines

2. At the meeting held on 13 August 2020, the joint SCEZD and SCVPD together with the EAP reviewed the then scientific development of COVID 19 vaccines and prioritization of target groups for COVID 19 vaccines in Hong Kong. The meeting recommended that vaccine procurement would be aimed at the whole Hong Kong population in the long run. In anticipation of a limited supply at the early stage when vaccines are available, a phased approach has to be taken with certain priority groups of the local population identified to be vaccinated first, in order to reduce morbidity and mortality and maintain essential services. Priority should be accorded to high-risk groups which are most vulnerable to the development of severe disease or death from COVID-19 infection and greater risks of exposure to the COVID-19 virus and/or transmitting the virus to susceptible and vulnerable individuals. Priority has been suggested to be accorded to healthcare workers, residents of residential care homes, Government frontline staff involved in health-related work, persons aged 60 years or above, and persons with chronic medical problems. The meeting recommended that the

priority groups to be vaccinated at a certain stage to be further worked out when information about the vaccine supply, data on the vaccines' safety profile and efficacy on various population subgroups becomes available.

3. On 11 December 2020, the Hong Kong SAR Government announced the latest development of COVID-19 vaccine procurement[1]. The Government is entering into agreement with vaccine developers of three vaccine candidates, namely Fosun Pharma/BioNTech for BNT162b2, Sinovac Biotech (Hong Kong) for CoronaVac and AstraZeneca for AZD1222. Characteristics of these three candidates are highlighted in Table 1. The Government is developing a territory-wide COVID-19 vaccination programme, with potential delivery strategies including vaccination centres, outreach sites, etc.

Table 1 - Characteristics of the three COVID-19 vaccines

Vaccine	**BNT162b2**	**CoronaVac**	**AZD1222**
Platform	mRNA	Inactivated	Adenovirus vector (non-replicating)
Dosing schedule (interval between 1st and 2nd dose)	2 dose (at least 21 days)	2 dose (14 or 28 days)	2 dose (4 to 12 weeks)
Packaging	Multi-vial (5)	*NA*	Multi-vial
Dilution required	Y (sodium chloride)	*NA*	*NA*
Shelf life	6 months at -75°C (±15°C); 5 days at 2-8°C	2-8°C (to be confirmed)	6 months at 2-8°C
Route of administration	IM	IM	IM

Emergency Use Approval for COVID-19 vaccines in Hong Kong

4. To facilitate timely access to COVID-19 vaccines without compromising proper regulatory decision-making, the WHO encourages countries' regulatory authorities to develop and implement regulatory pathways to use a risk-based approach to assess the quality, safety and efficacy of vaccines. Emergency approval, and/or expedited fast-track regulatory pathways should be in place as part of pandemic preparedness[2]. In Hong Kong, given the nature of the threat from COVID-19, the Government has put in place a legislative framework (Cap 599K) to enable the public to gain early access to promising vaccines when those products have not yet received full registration approval. An Advisory Panel on COVID-19 Vaccines (AP), comprising experts from relevant fields and sectors, has been set up to advise the Secretary for Food and Health on the authorization of COVID-19 vaccines for emergency use based on the available data concerning safety, efficacy, quality and scientific evidence, and on matters related to administration of the vaccine(s). Healthcare providers should refer to details regarding use of the individual product advised by the AP.

Recommendation

5. The joint SCZED, SCVPD and EAP convened on 7 January 2021, in advance of the completion of the AP's review of the Emergency Use Approval applications, to provide interim recommendations to the Government on allocation of initial doses, and on COVID-19 vaccines for use in Hong Kong, subject to the approval of emergency use by the Government. The interim recommendations might be updated based on additional safety and efficacy data from phase III clinical trials, international developments and conditions of the Emergency Use Approval.

6. The current recommendation focused on BNT162b2 and AZD1222, which is expected to be available in Hong Kong in the first and third quarter of 2021, based on the latest available data and information as of 7 January 2021. Recommendation on CoronaVac, which is expected to be delivered to Hong Kong in January 2021, will be updated should more clinical information become available.

Prioritization

7. While the COVID-19 vaccination aims to cover the whole Hong Kong population in the long run, COVID-19 vaccines available in early 2021 will be insufficient to cover the entire population. It would also be infeasible to vaccinate the whole population over a short time period. It is important to identify the highest priority groups to be vaccinated in the first phase, before moving to subsequent phases when vaccines will be offered to an increasingly larger part of the population. The optimal prioritization depends on the objective of the vaccination strategy, as well as the characteristics of the vaccine, in particular its efficacy against infection and onward transmission. The best use of available vaccine will also be dependent on the epidemiological scenario, in terms of the degree of COVID-19 ongoing transmission and burden in the local community.

8. In order to interrupt community transmission, vaccinating a sufficiently large proportion of the population with a vaccine highly effective at preventing infection and transmission is needed. The available evidence from phase III clinical studies of BNT162b2 and AZD1222 showed that the vaccines are efficacious in preventing symptomatic COVID-19 diseases. There is limited efficacy data on their effect in preventing asymptomatic SARS-CoV-2 infection, and a lack of data on reducing transmission. At the start of the vaccination programme, there is unlikely sufficient evidence on the effects of vaccination on transmission. In addition, vaccine availability will be limited and a sufficiently high level of vaccine coverage to interrupt community transmission would be difficult to achieve in the initial phase of the vaccination programme.

9. Hong Kong is currently experiencing community transmission of SARS-CoV-2. Taking into account the nature and supply of vaccines available at this stage, and the local epidemiology and disease burden, it justifies an initial focus on direct reduction of mortality and severe morbidity for the most at-risk; and protection of health and social care system.

10. Current scientific evidence strongly indicates that increasing age is the single greatest risk of mortality from COVID-19, and the risk increases exponentially with age. This trend was also reflected in our local data (persons aged 60 or above represented up to 95% of local mortality with crude case

fatality ratio: 30-59: 0.2%; 60-69: 1.4%; 70-79: 7.4%; 80+: 26.0%)[1]. In particular, those living in residential care homes (RCH) for older adults are disproportionately affected by COVID-19. They are in general at higher clinical risk of severe disease and mortality. In addition, the closed congregate settings facilitate transmission of infection, and increase the risk of major outbreaks According to the local data[2], for persons aged 60 years or above, those who are residents at RCHE/RCHDs were found to be at higher risk of severe outcomes and death compared to community-dwelling elders, with a two-times higher odds of severe COVID-19. The case-fatality ratio for cases involving residential care homes for the elderly (RCHE)/ residential care homes for persons with disabilities (RCHD) residents was about 18%. In larger outbreaks at RCHE/RCHD settings, the attack rate among residents ranged from 20% to 92%. It is considered that older adults residing in care homes should be the highest priority for vaccination. Staff of RCHE/RCHD should be vaccinated alongside. In addition, other institutionalized facilities with closed settings are also at increased risk of outbreaks; and the residents and staff should also be considered as a priority group, even though they may not be at same level of risk as institionalized elders.

11. Frontline health and social care workers are at increased risk of exposure to infection with COVID-19; and of transmitting that infection to susceptible and vulnerable patients in health and social care settings. Vaccination of healthcare workers protects the health and social care service, and improves the resilience of the healthcare system. Protecting the health and social care workers from infection would also reduce the risks of having vulnerable patients / elders exposed to infected care workers.

12. Apart from frontline health and social care workers, some other occupational groups which are at increased risk of exposure to COVID-19 (e.g. unable to maintain effective social distancing in performing work-related duties) AND are critical for maintaining essential societal functioning (such as first responders, transport workers, etc.) could also form part of the programme. The Joint Scientific Committee-EAP has advised on the broad principles, but would not deliberate on the detailed identification of these groups.

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[1]Based on 7,472 of 7,722 cases reported from 23 January to 15 December 2020 who were Hong Kong residents, fatality outcome as of 5 January 2021.
[2]Based on 7,472 of 7,722 cases reported from 23 January to 15 December 2020 who were Hong Kong residents.

13. The groups recommended in order of vaccination priority is outlined at Table 2.

14. COVID-19 is the first vaccination programme in Hong Kong targeting the entire population involving complex logistics. Other operational or practical considerations might require a flexible approach in vaccine deployment at local levels, with due attention to various implementation issues such as vaccine product storage capacity, availability of trained personnel of a certain setting for vaccination delivery, transport and administration constraints, and availability of suitable approved vaccines, etc.

Table 2. Proposed priority groups for COVID-19 vaccination in Hong Kong, in order of vaccination

Priority group	Considerations	Recommendation from overseas health authorities[‡]
1 Residents and staff of Residential Care Homes and other Institutionalized Facilities[a]	● Long term care facilities (LTCF) residents at high risk for infection and severe illness from COVID-19, because of their age, high rates of underlying medical conditions, and congregate living conditions. ● High attack rate (20%-92%) in RCH and residents have high case fatality ratio (18%). ● Long-term care setting can be high-risk locations for COVID-19 exposure and transmission. Care home staff have the potential for direct/ indirect exposure to cases/ infectious materials; and are at risk of transmitting the disease to vulnerable individuals. ● Immunizing RCH staff may also benefit from reducing transmission to vulnerable residents. ● Other institutionalized facilities with closed setting are also at increased risk of COVID-19 outbreaks.	***LTCF (e.g. RCHE/RCHD)***: Highest priority in UK, and included in first phase of vaccination in US. Also included in Stage 1 priority groups in Canada. ***Other congregate settings***: Stage 2 priority groups in Canada and early phases in US. Also included in priority group in Australia.
2 Workers in healthcare settings and essential services	*Workers in health care settings* ● Protection of healthcare personnel is critical to preserve capacity to care for patients with/combat COVID-19 or other illness; to maintain resilience of health care system particularly while hospitals are under pressure; ● Healthcare personnel are exposed to COVID-19 due to their professional activity. They are in contact with patients and vulnerable individuals at high risk of severe COVID-19, and are at increased risk of transmitting infection to susceptible patients in health settings. ● Potential benefit in preventing nosocomial transmission. *Workers in other essential services* ● Protection of occupational groups which are at increased risk of exposure to COVID-19 AND which are critical for maintaining	High priority in US and UK. Also included in priority groups in Canada and Australia.

			society effective functioning to ensure that the essential services are not disrupted	
	Persons Aged 60 Years or Above (in descending age)	●	Increasing age is one of the most significant risk of mortality from COVID-19; and case fatality ratio increased with age. ● Vaccinating older people offers direct protection against developing severe disease (primary objective); and may alleviate the pressure in healthcare sector through reducing the admission to hospitals and ICU (secondary objective).	Included in the first phase in UK and Canada, and in proposed Phase 1c in US (behind health care workers, RCH residents and essential workers)
3	Persons with Chronic Medical Problems aged between 16 and 59 years	●	Persons with chronic medical problems are at higher risk of severe outcomes and death as the odds of severe COVID-19 was 2 times higher in persons with chronic medical problems than those without (adjusted OR:2.2 95% CI 1.8– 2.7)	Younger adults with risk factors of severe COVID-19 were among the higher priority group in UK, Australia and US. The priority was lower than RCH residents (in both UK and US) and older adults aged 65 years or above (UK)[b].

a) Including Residential Care Homes for the Elderly (RCHE), Residential Care Homes for Persons with Disabilities (RCHD) and persons residing/ working in other institutionalized facilities (such as correctional institutions).

b) UK JCVI recommended those clinically extremely vulnerable individuals as the 4th whilst those aged 16 to 64 years with underlying health conditions as the 6th in the priority list.

15. The considerations with regard to the vaccination priority is summarized below:

Order 1

Residents and staff of Residential Care Homes and other Institutionalized Facilities: High attack rate and high mortality ratio in RCH is observed in local setting as well as in other places[3], which could be associated with factors including congregated living conditions in institutional setting, the higher vulnerability of residents, and difficulties in complying with infection control measures due to their age and health conditions. Although there are only limited efficacy data of COVID-19 vaccines in preventing transmission, vaccinating staff in RCH would reduce their risk of symptomatic COVID-19 disease and form part of an integral strategy in preventing COVID-19 in this setting. Even a small reduction in transmission arising from vaccination would add to the benefits of vaccinating this population, by reducing transmission from the care workers to multiple vulnerable patients in the long-term care facilities and other staff members. In addition, as other institutionalized facilities with closed setting are also at increased risks of COVID-19 outbreaks, the residents and staff in such settings should also be considered as a priority group

Order 2

(a) Workers in health care settings and other essential services: Health care workers (staff and alike students) are at higher risk of exposure to SARS-CoV-2 infection and of transmitting the infection to vulnerable patients in health care settings, and are considered a high priority for vaccination. Vaccination would reduce COVID-19 morbidity and maintain the resilience of the health care system. If the vaccines are effective in preventing SARS-CoV-2 infection, transmission of the virus in health care settings would also be reduced. Apart from workers in health care settings, protection of occupational groups which are at increased risk of exposure to COVID-19 AND which are critical for maintaining society effective functioning, would ensure that the essential services are not disrupted.

(b) Persons Aged 60 Years or above (in descending age): Both local and

overseas data showed that advanced age is the most significant predictor of deaths from COVID-19. According to local data from Jan to 15 December 2020, patients aged 80 years or above had the highest case fatality ratio (26.0%), followed by patients aged 70-79 years (7.4%). The risk of developing severe COVID-19 disease increased significantly across age groups, especially older persons aged 60 or above. In addition, the prevalence of co-morbidities increase with age. Phase III clinical study of BNT162b2 showed that the vaccine was effective in preventing symptomatic COVID-19 in older adults (VE among those 65+: 94.7% (95%CI 80.6-98.8))[4]. Older people is considered a priority group for vaccination, in order of descending age. Current evidence indicates that the risk of mortality from COVID-19 increases exponentially with age. In addition, age-based programme is a practical approach, is easier to implement and to communicate, and might achieve higher vaccine uptake. The primary objective of vaccinating older people is direct protection against developing severe disease. A secondary objective, particularly in an initial period of limited vaccine supply, may be to alleviate the pressure on the healthcare sector by reducing the number of people admitted to hospital and intensive care units.

Order 3

Persons with Chronic Medical Problems aged between 16 and 59 years:
Individuals with certain underlying health conditions (pre-existing conditions) are at higher risk of severe morbidity and mortality from COVID-19 compared to healthy peers. Phase III clinical study of BNT162b2 showed that 2-dose vaccination conferred comparable protection in vaccine recipients with or without risk factors[5]. Although stratified efficacy analysis is not available from the phase III study of AZD1222, at least 10% of their participants had different comorbidities such as cardiovascular disease, respiratory disease and diabetes and significant protection was shown to be conferred by the vaccine. Targeting individuals with pre-existing conditions known to be associated with increased risk of severe COVID-19 disease will reduce hospital admission, ICU admissions and mortality, which may include the following clinical conditions: having cancer, cardiovascular disease, diabetes mellitus, chronic respiratory diseases, hypertension, immune diseases, kidney disease and obesity (body mass index 30 or above).

Recommendations on use of BNT162b2 and AZD1222

Indications

16. BNT162b2 is a COVID-19 mRNA vaccine indicated for active immunisation against COVID-19 caused by SARS-CoV-2 in individuals aged 16 years or older.

17. AZD1222 is a recombinant, replication-deficient chimpanzee adenovirus vector encoding the SARS-CoV-2 Spike (S) glycoprotein indicated for active immunisation against COVID-19 caused by SARS-CoV-2 in individuals aged 18 years or older[6].

Dosage and Dosing Schedule

BNT162b2

18. BNT162b2 should be administered intramuscularly after dilution and each dose should consist of 30 micrograms of BNT162b2 RNA embedded in lipid nanoparticles.

19. The recommended schedule of BNT162b2 consists of 2 doses administered at least 21 days apart. Currently there is limited information on the safety, immunogenicity and efficacy of receiving BNT162b2 outside the recommended schedule.

20. Analysis of the phase III efficacy data of BNT162b2 showed that it was feasible to administer second dose from 19 to 42 days. The National Advisory Committee on Immunization (NACI) of Canada recommends a minimum interval of 19 days, authorized interval of 21 days and alternate interval of 28 days[7]. The US CDC allowed a grace period of 4 days[8] (i.e. second dose administered between day 17 and 21 are considered valid) although there was no clear indication on whether invalid second dose has to be repeated. On the other hand, if more than 21 days have elapsed since the first dose, the US CDC and Health Canada both recommend the second dose to be given at the earliest opportunity without repeating the series.

AZD1222

21. AZD1222 should be administered intramuscularly and each dose (0.5mL) should consist of 5 x 10^{10} viral particles. The recommended schedule consists of 2 doses and the second dose should be administered between 4 and 12 weeks[6].

22. Thus far, clinical trials on BNT162b2, AZD1222 and CoronaVac are limited to the exclusive use of the same vaccine. There are no data on the interchangeability of COVID-19 vaccines. Given the three COVID-19 vaccines available to Hong Kong were developed based on different technology platforms, individuals should complete their vaccination series with the same vaccine.

23. Until further information on duration of protection and alternative schedules involving different COVID-19 vaccines are available, further doses/ booster with the same or other COVID-19 vaccine is currently not recommended. Participants of COVID-19 vaccine clinical studies (whether local or overseas) should follow the recommendation from the investigators regarding completion of their COVID-19 vaccination series.

Contraindications

24. Individuals who have history of severe hypersensitivity to a previous dose of the same COVID-19 vaccine, the active substance or to any of the vaccine components should not receive BNT162b2 or AZD1222. Those who have history of severe hypersensitivity to polyethylene glycol (PEG) and polysorbate** should not receive BNT162b29.

25. Anaphylaxis refers to a severe and immediate allergic reaction that include clinical signs and symptoms such as hives, nausea, dizziness, hypotension (abnormally low blood pressure), swelling, or wheezing (respiratory distress)10. From 14 to 23 December 2020, a total of 1,893,360 doses of BNT162b2 were given as first dose in the U.S. Among adverse events reported to their Vaccine Adverse Event Reporting System (VAERS), 21 of these reports were determined to be anaphylaxis following BNT162b2 vaccination, corresponding to a rate of 11.1 per million doses administered 11. According to the US CDC, follow-up information was available for 20 of these cases and all had recovered or had been discharged home. 17 of these 21 cases (81%) had a documented history of allergies or allergic reactions, and seven had a history of

** BNT162b2 contains PEG. Although polysorbate is not contained in BNT162b2, it is closely related to PEG.

anaphylaxis. Anaphylaxis occurred shortly after vaccination for these cases (interval from vaccination to onset of anaphylaxis: median 13 minutes (range: 2 to 150 minutes)).

26. Anaphylaxis may occur following COVID-19 vaccination and measures to manage anaphylaxis[10] should be in place and immediately available, irrespective of the vaccination settings. All persons should be observed for 15 minutes after vaccination. Those with a history of immediate allergic reaction of any severity to a vaccine or an injection, and those with a history of anaphylaxis due to any cause should be observed for 30 minutes. Emergency equipment for appropriate medical treatment for severe allergic reactions must be immediately available in the event that an acute anaphylactic reaction occurs following administration of a COVID-19 vaccine) should be available in all vaccination settings. Health care professionals should give immediate attention and management to vaccinees suspected of anaphylaxis, and transfer patients to accident and emergency departments of public hospitals for further assessment and management. Doctors should report anaphylaxis and other adverse events following vaccination according to prevailing pharmacovigilance guidance[12]

Precautions

27. COVID-19 vaccination should be delayed for individuals suffering from acute febrile diseases. For individuals with laboratory confirmation of COVID-19 and under clinical care for the disease, vaccination should be deferred until the patients are considered fully recovered by frontline doctors and four weeks after symptom onset or first tested positive for asymptomatic cases[13].

28. The available safety and efficacy data of BNT162b2 and AZD1222 were based on clinical studies in individuals aged 16 and 18 years or above, including older adults[5]. There are no or limited data on the use of the vaccine in pregnancy and lactation, and children and adolescents. Therefore, Both BNT162b2 and AZD1222 are currently not recommended in these individuals[8]. However, vaccination with BNT162b2 and AZD1222 for these individuals may be considered after consultation with doctors on the risk and benefit of vaccination and their clinical conditions.

29. Given no known effect on BNT162b2 and AZD1222 vaccination on fetus and newborns/ infants, COVID-19 vaccines are not routinely recommended during pregnancy, unless the woman is considered at very high risk of SARS-CoV-2 exposure and subject to very high risk of COVID-19 complications. If a

woman finds out she is pregnant after COVID-19 vaccination, termination of pregnancy is not recommended and she should be offered the second dose, if applicable, as soon as after pregnancy[13].

30. While COVID-19 vaccination is not routinely recommended for breastfeeding women, those with high clinical need for protection against COVID-19 may be offered vaccination. Discussion with their doctors on the potential developmental and health benefit of breastfeeding as well as on the information about absence of corresponding safety data is advised.

31. There are limited data on the use of BNT162b2 and AZD1222 in immunocompromised individuals, and immune response may be diminished. Immunocompromised individuals may receive COVID-19 vaccine unless contraindicated.

32. Individuals with increased risk of bleeding, such as those who receive anticoagulant therapy or those with a bleeding disorder, may be at higher risk of adverse events to vaccination with COVID-19 vaccines that require intramuscular injection. These individuals are advised to discuss with their doctors on the potential risk and benefit, as well as the optimal timing and route of COVID-19 vaccination[14].

33. Any inadvertent administration of COVID-19 vaccine should be reported according to prevailing pharmacovigilance guidance[12].

Other considerations for use of COVID-19 vaccines

Prior infection of COVID-19

34. While there are limited safety and efficacy data of BNT162b2 and other COVID-19 vaccines in individuals previously infected with COVID-19, prior COVID-19 infection is not considered as a contraindication to COVID-19 vaccination. Phase III clinical study of BNT162b2 included individuals with previous COVID-19 infection for which vaccination appeared safe and efficacious. However, stratified vaccine efficacy estimates among those with and without prior infection was not available for both BNT162b2 and AZD1222 and it is unclear whether and how pre-existing immunity from prior infection contributed to the observed protective effect.

35. Reinfection of COVID-19 is rare. Individuals previously infected with

COVID-19, including those with serological evidence, could receive COVID-19 vaccine if indicated. Laboratory testing of COVID-19 (PCR or serology) in clinically well individuals is not routinely required before or after administration of COVID-19
vaccines[7,8].

Individuals exposed to SARS-CoV-2

36. There is currently no evidence on the safety and efficacy of COVID-19 vaccination as post-exposure prophylaxis. Two doses are required for the three COVID-19 vaccines available to Hong Kong and the time to complete the vaccination series would exceed the common incubation period of COVID-19. COVID-19 vaccines are currently not recommended as post-exposure prophylaxis.

37. Considering the risk of developing COVID-19 diseases in individuals exposed to SARS-CoV2 and potential onward transmission of the infection, COVID-19 vaccination should be deferred until after appropriate quarantine period ends as suggested by health care professionals.

Administration with other vaccines

38. Thus far there has been no interaction studies on the three COVID-19 vaccines with other prophylactic vaccines and/ or medications. In general, inactivated vaccines can be administered concurrently whereas an interval of 28 days is usually recommended for administration of live vaccines[15]. There is currently no consensus on the interval of co-administration of mRNA vaccine or non-replicating adenoviral vector vaccine with other vaccines. In accordance with interim guidance published by the US CDC, as a precaution, administration of COVID-19 vaccine 14 days before or after another prophylactic vaccines would allow clearer ascertainment of potential adverse events[8]. Inadvertent administration/ co-administration of COVID-19 vaccine with another vaccine shorter than this interval does not require repeating for either vaccine[8].

39. There is increasing evidence that co-circulation of SARS-CoV-2 and influenza viruses could have a significant impact on morbidity and mortality, and poor outcome in co-infected individuals[16]. In the context of the global pandemic of COVID-19, it is particularly important to ensure people who are at greater risk from infections or complications of both influenza and COVID-19, such as health care workers and older adults, can access and receive seasonal influenza vaccine (SIV)[17]. SIV can reduce the risk of influenza

infection and related complications, which could relieve the burden on healthcare system during the COVID-19 pandemic. Recommendations on SIV for the 2020-21 Season in Hong Kong, including the priority groups recommended, remains in effect[18].

Antibody-dependent enhancement (ADE) and vaccine associated enhanced respiratory diseases (VAERD)

40. Vaccine-mediated disease enhancement (i.e. a vaccine that results in increased disease severity if the subject is later infected by the natural virus) including antibody-dependent enhancement (ADE) and vaccine associated enhanced respiratory diseases (VAERD) are potential concerns of newly developed COVID-19 vaccines and are recommended to be part of benefit-risk assessment[19]. ADE occurs when non-neutralizing antibodies facilitate viral infection of cells instead of protecting the host and contribute towards an exacerbated pathology, and was observed in animal models for SARS. VAERD on the other hand, is a distinct clinical syndrome involving virus-antibody immune complexes and TH2-biased responses that occurred in young children in the 1960s when whole-inactivated virus vaccines for measles and respiratory syncytial virus (RSV) were tested[20]. Although phase III clinical studies of candidate COVID-19 vaccines often involve large number of participants in excess of 10,000, rare adverse events such as ADE and VAERD would require continuous monitoring when the vaccines are administered in mass.

Impact of vaccine delivery on non-pharmaceutical intervention

41. The development and use of safe and effective vaccines against COVID-19 is considered the most promising option for containing the pandemic in the long term. At the current phase of the vaccination programme, there is limited evidence on the effects of vaccination on infection and transmission of infection; and there are constraints in vaccine availability. Population level protection will not be achieved in the short term. Vaccination is only one of the tools in the overall public health response to COVID-19. There is a need to continue public health strategies on non-pharmaceutical interventions, including social distancing, good hand hygiene and wearing a mask in public, to reduce the risk of transmission.

Further work

42. Based on currently available evidence from immunogenicity data, there is no immunological correlate of protection determined for the virus. There also remains key knowledge gaps on understanding the safety, immune responses and effectiveness of COVID-19 vaccine, including the duration of protection, responses across different subgroups (e.g. immunocompromised, children and adolescents, pregnant and lactating women, those who are seropositive for SARS-CoV-2 or other coronaviruses), especially if there is substantial changes in the genetic and phenotypic characteristics of the circulating strain[7]. Efforts are to be made to ensure close and continuous monitoring on the safety, effectiveness and coverage of the vaccines; as well as to improve knowledge and understanding about the risk and benefit on use of the vaccines. For instance, the US FDA will recommend surveillance of Bell's palsy for BNT162b2 and Moderna as there was a numerical imbalance between the vaccine and control groups[21]. For AZD1222, 2 and 1 cases of transverse myelitis were reported in the vaccine and control group respectively[22]. The causality relationship of these adverse events are to be ascertained by corresponding authority and it is important to carry out ongoing safety surveillance. There is also no information about safety and effectiveness of off-label schedules (e.g. use of half-dose, prolonged intervals between doses).

43. Since COVID-19 is a novel disease, there are several unknowns. Viral antigenic drifts could generate immune escape variants. These aspects also need to be followed up and updated according to the emerging evidence.

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