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Global updates on COVID-19 and other diseases Sarawak Infectious Disease Centre (SIDC)

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Summary

- China is prepared to face an uptick in COVID-19 cases during the festive season.
- The US has reported further declines in COVID-19 markers.
- Denmark continues to track COVID-19 vaccination rates; however, it has ceased to determine where its residents get them from.
- The bivalent vaccines were proven to protect children from severe COVID-19.
- More evidence has suggested that mRNA vaccines are safe for pregnant mothers and their babies.
- Bacterial vaccines will be the future of the fight against resistant strains of bacteria.
- Dengue continues to plague Brazil and Malaysia.
- The outbreak of the vaccine-preventable disease measles highlights vaccine equity and the need to address concerns about vaccine use and vaccine hesitancy.
- Zoonotic disease such as Kyasanur Forest Disease and pneumonia from *Pasteurella multocida* highlighted the need for more investigations and vigilance for both scientist and clinicians.
- A new viral-like particle, called "Obelisks", associated with human cells and the microbiome has been described, but its function is yet unknown.

1.0 Situational summary: cases and related issues

1.1 Asia-Pacific and Southeast Asia

China

The National Health Commission (NHC) reported that at present, the COVID-19 epidemic is "at a low level" in China. However, recent surveillance data showed positive case reports have increased slightly which suggests that the epidemic is rising; the cause of which is due to the mass inter-regional as well as international movement or travel, and the increase in crowds gathering around the Spring Festival. According to the Chinese CDC, local cases are caused by the dominant JN.1 variant of interest (VOI).

Influenza has shown a downward trend. Other respiratory diseases, including mycoplasma, adenovirus, and respiratory syncytial virus, are reportedly at a low level. Flu is expected to fall to a low level around the Spring Festival holiday (11-17 February). Data from the CDC has suggested that there has been a general decline in acute respiratory disease cases since the peak in early December 2023. The diagnosis and treatment of respiratory diseases in outpatient and emergency



departments of level II medical institutions^{Footnote1} and above continued to remain stable. However, it is expected that the "epidemics of multiple respiratory diseases" will continue to spread during the festive holidays.¹

1.2 The Americas

The US

The US's respiratory virus activity remained elevated last week. Flu levels rose in some regions of the country, partly due to a slight rise in influenza B activity, which is sometimes seen in the latter half of the flu season. In general, hospitalisations for flu decreased and were highest in seniors, followed by adults ages 50-64 years and children ages 0-4 years.²

According to the CDC COVID-19 markers, both main severity indicators (hospitalisations and deaths) declined last week. While it declined 10% compared to the week before, hospitalisations remain elevated in older adults and infants < 12 months old. Deaths declined by 6.1%.³ National wastewater levels remained high though declining, with some parts of the country showing an upward trend.^{4 5}

1.3 Europe and the UK

Denmark

In January 2024, the Statens Serum Institut (SSI) reported that the widespread infection of 5 different respiratory diseases, including COVID-19 in Denmark in late autumn/early winter 2023 has peaked and was on a decline.⁶ The institute also reported that the variant updated COVID-19 vaccine (monovalent against XBB.1.15 sublineage) that was offered in autumn was effective; it reduced the risk of severe disease (hospitalisation) by 75%.⁶⁷

Earlier in October 2023, COVID-19 was reclassified from being "dangerous to public health" to "infectious disease" (at par with influenza) by the Danish Health Authority. ⁸ The government also made significant changes to its vaccination policy; from November 2022 until October 2023, those who elected to get vaccinated or boosted against COVID-19 could do so at government vaccination centres for a "modest" fee. Free vaccination is only for people in targeted groups or people in high-risk groups. However, this ended on 15 January 2024.^{9 10}

¹ The Classification of Hospitals (COH) divided hospitals into Grade I, II, and III hospitals according to their functions and roles. Grade I hospitals include community health centres and township health centres that directly provide prevention, medical care, and rehabilitation services to residents. Grade II hospitals are secondary hospitals that provide comprehensive medical services to a region and undertake some teaching and scientific research tasks. Grade III hospitals are tertiary hospitals that provide high-level specialised medical services and undertake advanced teaching and scientific research tasks. Each has a different impact on patient's medical outcome.⁴³



Pharmacies and private clinics were expected to fill in any gaps as a resource for COVID-19 vaccination. However, there seemed to be some problems in accessing the doses as not all pharmacies or private clinics stock up on the vaccines, and the nearest facility to do so may be some distance away.¹¹

As of 30 January 2024, approximately 1.1 million people (19% of the population) had received a COVID-19 vaccine during the 2023-2024 (autumn) season in Denmark.¹² However, the SSI is unable to determine how many of those were through the public vaccination programme and how many were paid for at private clinics.¹¹

2.0 Outcome

2.1 Bivalent COVID-19 vaccines protect children, update

In the latest update based on the 2022/2023 respiratory season, the bivalent mRNA COVID-19 vaccine was found to be effective for children; there was a 54% effectiveness against infection and 49% against symptomatic COVID-19 in children and adolescents ages 5-17 years old.^{13 14}

Similar findings were reported by the CDC in adults for the latest monovalent version of the vaccine. $^{\rm 15\ 16}$

2.2 More evidence supporting the safety of maternal COVID-19 vaccination

A large population-based cohort study that looked at all data from June 2021 until January 2023 from Sweden and Norway (n=196,470 newborn infants) provided more evidence maternal mRNA COVID-19 vaccines are safe for newborns. It found that newborns whose mothers received at least one mRNA COVID-19 vaccine during pregnancy had no worse outcomes^{Footnote2} than those whose mothers did not get the vaccine during pregnancy.¹⁷

The unadjusted mortality rates for vaccine-exposed neonates were similar to that when adjusted: the mortality rates for vaccine-exposed neonates in the two countries were about half of those for unexposed neonates (adjusted odds ratio, aOR 0.68, 95% CI: 0.50-0.91). The study also found that neonates exposed to a maternal COVID-19 vaccine had lower odds for non-traumatic intracranial haemorrhage (aOR 0.78, 95% CI: 0.61-0.99), and also lower odds of hypoxic-ischemic encephalopathy with maternal vaccination in the second trimester (aOR 0.73, 95% CI: 0.55-0.96).

Of the neonates who were exposed to the vaccine, 48% were exposed to at least one COVID-19 vaccination with an mRNA vaccine during pregnancy, with most being

² Report 2024-R3, Section 4.4 highlighted the positive results of mRNA vaccination on pregnant mothers based on a small cohort in the US.



exposed to one or two vaccinations; 80% were exposed to the Pfizer-BioNTech BNT162b2 (Comirnaty) vaccine and approximately 20% to the Moderna mRNA-1273 (Spikevax) vaccine. Overall, 32% of the infants were exposed during the first trimester, 43% during the second trimester, and 24% during the third trimester.

The authors reported that people who were vaccinated during pregnancy in both Sweden and Norway were older, of Nordic origin, had more education, more often nulliparous, and had more comorbidities than pregnant people who did not get vaccinated (P<0.001). Vaccine-exposed infants were less likely than infants with no exposure to the COVID-19 vaccine to be preterm, small for gestational age, or have decreased Apgar scores.

The study and the results are "of great importance for healthcare professionals offering counselling, authorities issuing recommendations, and for anyone who will become pregnant in the future".¹⁸

In October 2023, a population-based retrospective cohort study from Canada found that maternal mRNA COVID-19 vaccination during pregnancy was associated with lower risks of poor neonatal outcomes, including neonatal death.^{19 20}

3.0 Planning

Vaccines as a future tool to fight antibiotic resistance

With the pipeline for new antibiotics weak and underfunded, vaccines could be the potential tool for preventing infections that drive antibiotic use and resistance. There are 61 vaccine candidates identified by the WHO based on a 2022 analysis of the clinical and preclinical pipeline of bacterial vaccines, while the proof of concept (for bacterial vaccine) exists as per the agency's list of licensed vaccines against bacterial pathogens including *for Salmonella enterica* ser. Typh; *Haemophilus influenzae* type B; and *Streptococcus pneumoniae*.²¹

The current pneumococcal conjugate vaccines (PCV), have been highly effective in reducing the prevalence of drug-resistant *S. pneumoniae* infections. Five years after its introduction, invasive pneumococcal disease caused by drug-resistant strains in children ≤ 2 years old was reduced by 84% in the US, and the rate of penicillin-resistant pneumococcal disease in children declined by 82% in South Africa – indicating the potential to reduce the burden of resistant infections.

In a recent report by *CIDRAP* (Center for Infectious Disease Research and Policy, University of Minnesota), a biotech hub in Minnesota has begun the development of a vaccine against two common pathogens, *Escherichia coli* and *Klebsiella pneumoniae*. These pathogens are linked to urinary tract infections (UTIs), and are a primary driver of antibiotics prescribing worldwide. The bacteria mainly afflict women – sometimes with repeated UTIs, thus prolonged use of antibiotics – and are



the cause of approximately 2.5 million infant deaths annually due to neonatal sepsis mainly in low- and middle-income countries (LMICs).²²

A study published in 2023 found that when given to expecting mothers, vaccines against *K. pneumoniae* could reduce neonatal sepsis deaths in many LMICs by 15%. The modelling-based study projected that the regions with the greatest reduction in neonatal sepsis deaths, namely sub-Saharan Africa and southeast Asia, would likely see the greatest reduction in newborn deaths from drug-resistant *K. pneumoniae*.²³

4.0 Others

4.1 Zoonosis

4.1.1 Kyasanur Forest Disease, India

Forty-nine cases of "monkey fever" or Kyasanur Forest Disease (KFD) have been reported from Karnataka state since January 2024. Most were from Uttara Kannada district followed by neighbouring Shivamogga and Chikkamagaluru districts. Twelve people out of 31 cases have so far been hospitalised in Uttara Kannada district. According to health authorities there, most cases were localised. Of all 49 cases reported, two died – the first, was an 18-year-old female, on 8 February 2024, while the second was a 79-year-old man, whose date of demise was not stated. Both were from different parts of the state.

The virus, KDFV, belongs to the Flaviviridae family. It causes haemorrhagic disease and is spread by *Haemaphysalis spinigerai* ticks. The ticks thrive on primates and can infect birds and mammals. Humans are accidental hosts when the KFDV is transferred from cattle grazing in the forests.

Teams from the health department as well as forest officials have been carrying out door-to-door awareness programmes about the precautions that must be taken. Authorities from neighbouring areas have been alerted to look for dead primates and cases of fever in humans. Those living in and around the forested areas were reminded to be more careful as they are at high risk of getting infected. The use of insect repellent is recommended. For people entering forested areas where monkey deaths have been reported, they were advised to cover up and wear shoes to avoid tick bites.

The KFD was first identified and described in 1957. It was named after Kyasanur Forest, in Karnataka (formerly Mysore) State, India, where it was first found. According to the Central Coastal Agricultural Research Institute (ICAR) in North Goa, symptom onset is between 3-8 days after a tick bite and may include fever, chills, frontal headaches, body pain, diarrhoea, and vomiting. It may progress to haemorrhagic manifestations (for example, blood in the vomitus, sputum, and



stools). Most patients recover within one or two weeks. However, some symptoms may relapse after a brief period of one to two weeks, which includes severe headache, mental disturbance, tremors, and vision problems.^{24 25 26 27}

4.1.2 Pneumonia from dog licks

A 71-year-old man from Spain almost died from pneumonia suspected to be from the licks of his pet dog. The patient, a person with comorbidities who was otherwise healthy, only sought medical attention after a week of fever, diarrhoea, coughs, and shortness of breath. Laboratory tests subsequently found that he had contracted *Pasteurella multocida*, a common bacteria found in a dog's mouth.^{28 29}

4.2 Dengue

4.2.1 Brazil

Brazil is facing an enormous outbreak of dengue fever in the current hot, rainy season – which could mean a coming surge in the mosquito-borne virus across the Americas. The surge has forced health authorities to take emergency measures including mass vaccination against the disease. There have been 364,855 cases reported in the first 5 weeks of the year – four times more than in the same period in 2023; there have been 40 confirmed deaths with 265 more being investigated.³⁰

The number of cases reported in Brasilia, located in one of the three most affected states which have declared a health emergency, has exceeded the total for the whole of 2023, with a rate of infection of 1,625 cases per 100,000 inhabitants, compared to the national average of just 170. The army has been deployed in the capital to help track breeding spots of the disease vector, *Aedes aegypti* mosquito, in homes and backyards wherever there is stagnant water. The Air Force has set up a field hospital in preparation for a surge in cases needing hospital care in Ceilandia, a densely-populated poor suburb of Brasilia.

In aid of controlling the disease, the Brazilian government bought 5.2 million doses of the dengue vaccine Qdenga (Takeda, Japan) with another 1.32 million doses provided at no cost to the government. Children 10-14 years old in the capital are targeted to be the first group to get vaccinated against dengue.

Rio de Janeiro and other cities that were preparing to celebrate The Carnival which started on 10 February 2024 have taken measures to prevent an epidemic. The Health Ministry has set up an emergency centre to coordinate operations against dengue across Brazil.

The current surge in dengue in Brazil as well as other locations in the southern hemisphere is fuelled by the El Niño phenomenon that brought increased rainfall.³¹ According to the WHO, this outbreak in Brazil is part of a large global increase in



dengue fever, with over 500 million cases and over 5,000 deaths reported last year from 80 countries in every region of the world except Europe.^{32 33}

4.2.2 Malaysia

Kementerian Kesihatan Malaysia (KKM) has confirmed an alarming 65% increase in dengue cases this year; there have been 18,247 cases reported within the 5 weeks of 2024 compared to 11,127 cases reported last year. At the same time, 9 deaths were reported compared to 6 last year.³⁴ The current cases were from a total of 180 areas across the country, the breakdown as follows: 143 in Selangor, 20 in Kuala Lumpur and Putrajaya, 7 in Negeri Sembilan, four in Perak, three in Penang, and one each in Pahang, Sabah, and Sarawak. According to authorities, the transmission of dengue was likely attributed to the festive season and school holidays.

Surveillance on chikungunya, a disease that shares the same vector, recorded a total of three cases up till week 5 of 2024, with the latest reported in the fifth week. No outbreaks were detected.

The public was called to adopt safety and preventive measures to mitigate the spread of the disease, which includes removing or destroying mosquito breeding sites, using insecticides or repellents, and to avoid being outdoors when the mosquito vector is active.

4.3 Measles

4.3.1 Sabah, Malaysia

Thirty cases of measles were reported in Penampang district in the first 5 weeks of the year. Of the total, 17% received at least one dose of measles vaccination, while 27% have never received any measles vaccine. Approximately 53% did not know their vaccination status, while 3% were not yet eligible for the vaccine. The majority of the total (87%), were Malaysians, and more than half (67%) were adults (\geq 18 years old).³⁵

A measles prevention programme was conducted to control the spread of the disease. It involved conducting a series of intervention programmes, including a full epidemiological investigation, laboratory and environmental investigation, health promotional activities, and supplementary immunisation activity (SIA). The SIA is typically conducted within a 1km radius of a measles outbreak locality with inoculation delivered to all targeted individuals no matter their vaccination status. The current programme included areas with low immunisation coverage and high-risk areas. As of 9 February 2024, 16 case localities have been identified for the SIA.



The authorities have successfully reached a 95% immunisation rate in Penampang using the monovalent measles-rubella (MR) or measles-mumps-rubella (MMR) vaccines in the SIA programme. Three-hundred and sixty-six children between the ages of 6 months and 15 years have been vaccinated, 231 (63%) of them Malaysians.

4.3.2 The UK

The UKHSA has warned that the number of cases of measles has continued to rise (Figure 1). ^{36 37}



Figure 1. Laboratory-confirmed cases of measles by month of onset of rash or symptoms were reported in London and England, from January 2023 to December 2023. Cases were confirmed through either local or reference laboratory testing. Data for December 2023 are provisional and subject to confirmation in the reference laboratory and are therefore depicted as dotted lines. The chart and its description were obtained from <u>Confirmed cases of measles in England by month, age and region: 2023 - GOV.UK (www.gov.uk)</u>

From October 2023 until February 2024, 465 cases were reported in England, the majority (71%) from the West Midlands. Most cases (66% or 306) were in children < 10 years old, while 25% were in young people and adults < 15 years old. The sharp rise was mainly driven by cases in Birmingham. According to health providers, most cases involved unvaccinated individuals and were linked to areas that were experiencing poverty and deprivation. Immunisation teams have been deployed to



provide access to the vaccines, and answer concerns regarding the vaccine while having to address the problem of language barriers. According to the UKHSA, the measles outbreak in the West Midlands continues to be a concern. In general, MMR vaccine uptake has been falling over the last decade with one out of 10 children starting school in England not protected.

The UKHSA declared measles a national health incident on 19 January 2024. The disease was declared eliminated in Britain more than 7 years ago.

4.3.3 Ireland

A man who contracted measles has died in a hospital in Ireland. According to the Health Service Executive (HSE), it was the first confirmed case in the country in 2024. According to the agency, four measles cases were reported in 2023, two in 2022, none in 2021, and 5 in 2020. No deaths were reported in any of those years. Public health teams and the Measles National Incident Management Team (IMT) were "taking all necessary public health actions (about) the case". HSE's Health Protection Surveillance Centre (HPSC) noted that since 2020, most confirmed cases of measles in Ireland reported recent travel to countries where outbreaks were ongoing.³⁸

Officials have reported that vaccination levels had declined < 90% nationally, and < 80% in some Irish counties – about 95% of the population needed to be vaccinated to prevent the disease from spreading.

4.4 Obelisks, a new virus-like entity discovered in humans

A new virus-like entity has been discovered in the human gut based on the analysis of sequence databases.³⁹ Obelisks are entities that have genomes seemingly composed of loops of RNA which consists of approximately 1,000 bases. Research has estimated almost 30,000 of them – all distinct from each other. Some of the obelisk sequences encoded proteins involved in RNA replication, making them more complex than viroids. Similar to viroids, and unlike most viruses, obelisks do not encode proteins that make up a shell/capsid. Obelisk sequences were found in 7% of human gut bacteria and in half the bacteria in the human mouth. It is yet unknown whether obelisks affect human health – if they could alter the genetic activity of their bacterial hosts, which in turn could affect human genes. Investigations are ongoing to further understand the relationship between the obelisks and human cells and the microbiome.^{40 41}



5.0 Implications for Sarawak according to the views of SIDC

More evidence is presented on the protective effect of the mRNA vaccine on mothers and babies. Knowing that mRNA COVID-19 vaccination is safe for both mother and child should encourage the uptake of the vaccine. The latest study based on two Scandinavian countries pointed out 'a bias'; those likely to get vaccinated were more mature and educated and of certain ethnicity. With this in mind, a strategy to encourage equitable vaccine uptake can be made, to help protect communities with low vaccine uptake.

The same goes for vaccine-preventable diseases such as measles. It may seem unusual for Malaysians to not have their MMR vaccinations. However, those in the far rural areas, including children who were not in the school system, would have missed theirs. High sustained vaccination coverage is central to eliminating endemic measles. Actively seeking out these pockets of communities as well as active disease surveillance can assist health promotional activities and supplementary immunisation activity (SIA) where needed.

There may be misleading information regarding measles as "Disease X". We are compelled to correct this. Measles is highly contagious among people who are not vaccinated – seen locally and elsewhere globally. It is also highly preventable with the existing vaccine and therefore has little pandemic potential.⁴²

Bacterial vaccines provide an economic rationale for investing in Antimicrobial resistance (AMR) mitigation strategies, where prevention is better than cure, as the cost of the latter can be much more than the former. These vaccines could help reduce or prevent infections, both susceptible and resistant, that lead to antibiotic use and misuse. The fewer antibiotics misused, the likelihood of reducing the chances of resistance is increased.²²

We were made aware of Kyasanur Forest disease (KFD) in 2023. The disease is associated with forests, monkeys, mammals, the tick vector, and humans. Visitors to Karnataka, popular with lush forests and animals, need to be aware of the local diseases including zoonotic diseases. Likewise, visitors to forested areas in the state. Clinicians in the state will also need to be aware of it – hence the importance of travel history.³ The spread of pathogens have be linked to travel to endemic regions/areas. The range of the ticks, and the susceptibility of the monkeys in Borneo to the virus (as a host), will need to be determined.

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