Weekly Evidence Report

Health Technology Assessment Philippines

31 Jan 2022 to 06 Feb 2022

Overview

The following report presents summaries of evidence the Department of Health (DOH) - Health Technology Assessment (HTA) Unit reviewed for the period of 31 Jan to 06 Feb 2022. The HTA Unit reviewed a total of **15 studies** for the said period.

Evidence includes **4 studies** on Epidemiology; **1 study** on Transmission; **2 studies** on Drugs; **6 studies** on Vaccines, **0 studies** on Equipment and Devices; **0 studies** on Medical and Surgical Procedures; **0 studies** on Traditional Medicine; and **2 studies** on Preventive & Promotive Health.

Sections

Evidence on Epidemiology

Local COVID-19 Tracker: https://www.doh.gov.ph/covid19tracker
Local COVID-19 Case Tracker: https://www.doh.gov.ph/covid-19/case-tracker

Date	Author/s	Title	Journal/ Article Type	Summary
01 Feb 2022	WHO Global	Weekly epidemiological update on COVID-19 - 01 February 2022	WHO Global (Situation Report)	• Globally, the number of new COVID-19 cases remained similar to that reported the previous week (24-30 Jan 2022), while the number of new deaths increased by 9%. • As of 30 Jan 2022, over 370 million confirmed cases and over 5.6 million deaths have been reported worldwide.
			WHO Global (Situation Report – *Regional Updates)*	• The Western Pacific Region reported the highest increase in number of new cases (37%), followed by the Eastern Mediterranean (24%) and the European (7%) Regions. • The number of new deaths continued to increase in the South-East Asia Region (41%), the Eastern Mediterranean Region (32%), and the region of the Americas (16%). The incidence of deaths in the European and Western Pacific regions remained similar to the past week.
			WHO Global (Situation Report – *SARS-CoV-2 variants of interest and variants of concern)*	• Currently, there is a rapid increase in transmission of the Omicron variant. Among the sequences uploaded to GISAID of specimens collected in the last 30 days, 93.3% were Omicron, 6.7% were Delta, and <0.1% were Gamma, Alpha, and Beta VOCs. • All other VOCs and VOIs continue to decline in all 6 WHO regions. • The Pango BA.1 lineage of the Omicron variant accounts for 96.4% of sequences submitted to GISAID as of 31 Jan 2022. Several countries have reported a relative increase in the BA.2 lineage of the Omicron variant, which differs from BA.1 in some mutations. Investigations on the the characteristics of BA.2, including its transmissibility, virulence, and immune escape are ongoing.

Evidence on Epidemiology (continued)

Evidence on Vulnerable Population Epidemiology

Date	Author/s	Title	Journal/ Article Type	Summary
03 Feb 2022	Nomah, D., Urueña, J., Llibre, J., Ambrosioni, J., Miro, J., Casabona, J.	HIV and SARS-CoV-2 Co-infection: Epidemiological, Clinical Features, and Future Implications for Clinical Care and Public Health for People Living with HIV (PLWH) and HIV Most-at-Risk Groups	*Curr HIV/AIDS Rep / Rapid review*	• This review of currently available clinical and epidemiological data of COVID-19 in persons living with HIV aimed to identify points for improvement in the management of SARS-CoV-2 and HIV co-infection in the clinical and public health perspective. • Across Europe, the incidence of COVID-19 in PLWH ranged from 0.3 to 5.7% person-years while the mortality rates among persons with SARS-CoV-2/HIV co-infection ranged from 1.9 to 29.0%. Patients were predominantly males, 38 to 56 years, and were more likely to belong to a lower socioeconomic class. • The use of antiretroviral therapy (tenofovir disoproxil and lopinavir/ritonavir) for the treatment of COVID-19 remains to be proven with strong evidence. • Rates of COVID-19 ICU admission among PLWH ranged from 3 and 22%, while COVID-19 hospitalization rates ranged from 17 to 33%. Clinical data have also suggested that HIV infection is a significant independent risk factor for severe/critical COVID-19 and mortality. However, it is to note that the presence of other comorbidities were reported in two-thirds of PLWH who had COVID-19. Other risk factors associated with severe outcomes were HIV-associated comorbidities, low CD4 cell count (< 200 cells), and unsuppressed HIV viraemia.

Evidence on Epidemiology (continued)

Evidence on Vulnerable Population Epidemiology

Date	Author/s	Title	Journal/ Article Type	Summary
02 Feb 2022	Monika, P., and Chandraprabha, M.	Risks of mucormycosis in the current Covid-19 pandemic: a clinical challenge in both immunocompromised and immunocompetent patients	*Molecular Biology Reports / Review*	• Mucormycosis, also known as "Black Fungus" or Zygomycosis, is a fungal infection that has been reported worldwide in people who have recovered from COVID-19. • The mortality rate of mucormycosis was reported to be 50-80% In COVID-19 patients. • The disease mainly affects immunocompromised persons including those with diabetes, haematological malignancy, organ and skin transplant and COVID-19. Some immunocompetent persons may be at risk of contracting mucormycosis, especially COVID-19 patients who received steroids as treatment for COVID-19. • Mucormycosis can be prevented with proper hygiene and nutrition, and can lead to better outcomes with proper and timely diagnosis. Treatment includes surgical debridement of infected tissue followed by first-line treatment with Amphotericin B.
03 Feb 2022	Khan, A., Schwalm, C., Wolfson, J., Levine, J., and Johnston, E.	COVID-19 in children with cancer	*Current Oncology Reports / Review*	• Among cancer patients of all ages with COVID-19, children have a lower rate of morbidity and mortality than adults. Only 4–9% of pediatric oncology patients had severe or critical COVID-19 compared to 55% of adult cancer patients. The COVID-19 mortality rate in pediatric cancer patients is 4%, and 55% in adult cancer patients. • Compared to the pediatric non-oncology population, data from the Pediatric Oncology COVID-19 Case Registry and the Global COVID-19 and Childhood Cancer Registry showed that pediatric oncology patients with COVID-19 have a much more severe clinical course overall and higher death rate. Additionally, reports of MIS-C in pediatric cancer patients with COVID-19 have been received; however, a comparison with non-oncology patients cannot be made due to issues with data collection.

Evidence on Transmission

Date	Author/s	Title	Journal/ Article Type	Summary
03 Feb 2022	Clyne, B., Jordan, K., Ahern, S., Walsh, K., Byrne, P., Carty, P., Drummond, L., O'Brien, K., Smith, S., Harrington, P., Ryan, M., and O'Neill, M.	Transmission of SARS-CoV-2 by children: a rapid review, 30 December 2019 to 10 August 2020	*Eurosurveillance / Rapid review*	• A total of 28 studies - 19 studies on household and close contact transmission, 6 studies on transmission of SARS-CoV-2 in educational settings, and 3 modelling studies estimating age-specific transmissibility of SARS-CoV-2 - were included in this review. The search period was from 30 December 2019 to 10 August 2020. • Across the 19 studies on household and close contact transmission, from a total population of 42,926 children, there were a total of 42,639 cases were a child was the index case that infected close contacts (predominantly family members). Transmission was more likely to come from older children rather than infants and younger children. • Regarding transmission of SARS-CoV-2 educational settings, the review detected 65 cases where a student was considered to be the index case and 183 additional infected contacts were identified from 14,003 close contacts. Transmission was more likely to occur in secondary school settings rather than preschool settings. • All three transmission modelling studies estimated lower rates of transmission from children and young people compared to adults. One study estimated that although children <10 years have an equal likelihood to infect at least one person they contributed less to the spread of SARS-CoV-2, infected fewer people, and have a lower secondary attack rate compared to the transmission capability of adults.

Evidence on Drugs

Date	Author/s	Title	Journal/ Article Type	Summary
31 Jan 2022	Vegivinti, C.T.R., Evanson, K.W., Lyons, H. *et al.*	Efficacy of antiviral therapies for COVID-19: a systematic review of randomized controlled trials	*BMC Infectious Diseases / Systematic review*	• This systematic review of RCTs published up to 04 Sep 2021 was conducted to assess the efficacy of current antiviral therapies for COVID-19. • A total of 31 studies involving 12,440 patients were included in the review. Antiviral treatments that were studied in the included RCTs were umifenovir, baloxavir marboxil, enisamium, favipiravir, lopinavir/ritonavir, remdesivir, ribavirin, sofosbuvir/ daclatasvir, sofosbuvir/ledipasvir, sofosbuvir/ravidasvir, and sofosbuvir/ velpatasvir. • Overall, antiviral therapies led to better patient recovery outcomes when administered early in the course of illness. However, no antiviral treatment was seen to be effective against COVID-19 mortality.
03 Feb 2022	Varikasuvu, S., Thangappazham, B., Vykunta, A., Duggina, P., Manne, M., Raj, H., Aloori, S.	COVID-19 and vitamin D (Co-VIVID study): a systematic review and meta-analysis of randomized controlled trials	*Expert Review of Anti-Infective Therapy / Systematic review and meta-analysis*	• Several studies have already associated low levels of Vitamin D with susceptibility to SARS-CoV-2 infection and severe COVID-19 outcomes. This SRMA was conducted to assess the efficacy of Vitamin D in the treatment of COVID-19. • A total of 6 RCTs involving 551 COVID-19 patients were included in the review. The overall pooled relative risk for all outcomes suggested the beneficial use of Vitamin D intervention in COVID-19 (RR = 0.60, 95% CI 0.40 to 0.92, Z = 2.33, p = 0.02, I^2 = 48%). • Additionally, the risk of SARS-CoV-2 infection was significantly lower in the intervention group compared to the placebo group (RR = 0.46, 95% CI 0.24 to 0.89, Z = 2.31, p = 0.02, I^2 = 0%). • It was concluded that Vitamin D supplementation in COVID-19 produced lower rates of ICU admission, mortality and RT-PCR positivity.

Evidence on Vaccines

Date	Author/s	Title	Journal/ Article Type	Summary
31 Jan 2022	Roberts, E., Gu, T., Mukherjee, B., Fritsche, L.	Estimating COVID-19 Vaccination Effectiveness Using Electronic Health Records of an Academic Medical Center in Michigan	*medRxiv / Test-negative case-control observational study*	• This test-negative case control study in Michigan, USA, estimated the vaccine effectiveness of two doses and a booster dose. The study consisted of 170,487 adult patients tested for or diagnosed with COVID-19 in 2021, which was dominated by multiple variants, including Omicron. • Vaccine effectiveness against SARS-CoV-2 infection and severe COVID-19 were higher for the mRNA booster compared to full vaccination in the 4th quarter of 2021 [VE against infection: 64.0% (61.1 to 66.7) vs. 87.3% (85.0 to 89.2) and VE against severe COVID-19: 78.8% (73.5 to 83.0) vs. 94.0% (89.5 to 96.6)].
01 Feb 2022	Bar-On, Y., Goldberg, Y., et al.	Protection by 4th dose of BNT162b2 against Omicron in Israel	*medRxiv / Prospective cohort*	• On Jan 2, 2022, Israel began administering the 4th dose of *Pfizer-BioNTech* to older adults ≥60 years and at risk-populations who received the 3rd dose at least 4 months prior. • This observational study spanning the Omicron-dominated period from Jan 15-27 aimed to compare the rate of infection and severe COVID-19 in those who received the 4th dose and those who have only had the 3 doses. • Compared to those who only had 3 doses and those had the 4th dose 3 to 7 days prior, the rate of confirmed infection was lower among individuals who received their 4th dose at least 12 days prior by 2.0 (95%CI: 2.0 to 2.1) and by 1.9 (95%CI: 1.8 to 2.0), respectively. Meanwhile, the rate of severe COVID-19 was lower by 4.3 (95% CI: 2.4 to 7.6) and 4.0 (95% CI: 2.2 to 7.5), respectively.

Evidence on Vaccines (continued)

Date	Author/s	Title	Journal/ Article Type	Summary
01 Feb 2022	Hviid, A., Hansen, J., Thiesson, E., Wohlfahrt, J.	Association of AZD1222 and BNT162b2 COVID-19 Vaccination With Thromboembolic and Thrombocytopenic Events in Frontline Personnel	*Annals of Internal Medicine / Retrospective cohort study*	• In this nationwide exploratory retrospective cohort study, the information of 355,209 Danish frontline HCWs were taken from national registers on vaccination and hospitalization. The study aimed to evaluate the risk of cerebral venous sinus thrombosis, splanchnic vein thrombosis, pulmonary embolism, deep venous thrombosis, arterial thrombosis, thrombocytopenia, and death following vaccination with *AstraZeneca* or *Pfizer-BioNTech.* • Compared to no vaccination, *AstraZeneca* was associated with a significant risk difference (RD) at day 28 for deep venous thrombosis (RD, 8.35 [95% CI, 0.21 to 16.49] per 100 000 vaccinations). The risk for CVST and thrombocytopenia following *AstraZeneca* were not significant. Meanwhile, *Pfizer-BioNTech* was not associated with the risk of any of the thromboembolic and thrombocytopenic events.
02 Feb 2022	Pratama, N., Wafa, I., Budi, D., Putra, M., Wardhana, M., and Wungu, C.	mRNA Covid-19 vaccines in pregnancy: A systematic review	*PLOS ONE / Systematic Review*	• In this systematic review involving 13 observational studies and a total of 48,039 pregnant women, provided evidence that mRNA vaccines can prevent future SARS-CoV-2 infection and did not show clear harm in pregnancy, delivery, or neonatal outcomes (no statistical significant difference between vaccinated and unvaccinated pregnant women). • In a subgroup analysis of studies that investigated transplacental antibody transfer, it was found that increased latency between vaccination and delivery was correlated with better antibody transfer and higher infant IgG levels. Additionally, a higher proportion of neonates were positive for IgG antibodies among those whose mothers received two doses of the vaccine [98.5% (65/67)] versus neonates whose mothers who only received one dose [43.6% (24/55)].

Evidence on Vaccines (continued)

Date	Author/s	Title	Journal/ Article Type	Summary
03 Feb 2022	Alexander, J., Kennedy, N., Ibraheim, H., Anandabaskaran, S., Saifuddin, A., Seoane, R., et al.	COVID-19 vaccine-induced antibody responses in immunosuppressed patients with inflammatory bowel disease (VIP): a multicentre, prospective, case-control study	*The Lancet / Prospective, case-control study*	• In this multicenter, prospective, case-control study, 362 adults with IBD treated with an immunosuppressive treatment regimens (thiopurines, infliximab, a thiopurine plus infliximab, ustekinumab, vedolizumab, or tofacitinib) and 121 healthy controls were recruited. The primary outcome, anti-SARS-CoV-2 spike protein antibody response, was measured using serum collected 53 to 92 days after the second dose. Geometric mean anti-SARS-CoV-2 spike protein antibody concentrations were significantly lower in patients treated with infliximab, thiopurine plus infliximab, and tofacitinib vs controls. No significant difference was seen in the antibody response of patients treated with the other treatment regimens vs controls. The study recommended that scheduling of the third dose or booster in patients with IBD could be personalised based on the patient's treatment regimen, and that patients taking anti-tumour necrosis factor and tofacitinib should be prioritized for vaccination.
03 Feb 2022	Petrelli, F., Luciani, A., Borgonovo, K., Ghilardi, M., Parati, M., Petro, D., Lonati, V., Pesenti A., and Cabiddu, M.	Third Dose of SARS-CoV-2 Vaccine: A Systematic Review of 30 Published Studies	*Journal of Medical Virology / Systematic Review*	• In this systematic review involving 2,734,437 individuals vaccinated with the booster, the reduction of the risk of infection ranged from 88% to 92%. • IgG seroconversion rates among immunocompromised patients (transplant recipients and cancer patients) increased from 39.4% before the third dose to 66.6 after vaccination. • The authors emphasized on the importance of a third dose to to protect against infection, severe disease, and death due to COVID-19.

NYT Coronavirus Vaccine Tracker:
https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html

Bloomberg Vaccine Tracker:
https://www.bloomberg.com/graphics/covid-vaccine-tracker-global-distribution/

London School of Hygiene and Tropical Medicine Vaccine Trial Mapper and Tracker:
https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/

ACIP Files: https://drive.google.com/drive/u/0/folders/1v-jd66qIIxnUkfzXWKqiD0mkVvqy_VvJ?pli=1

Note. Studies that have not been peer-reviewed are highlighted in red.

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Evidence on Medical and Surgical Procedures

Date	Author/s	Title	Journal/ Article Type	Summary
03 Feb 2022	Henderson, L., Canna, S., Friedman, K., Gorelik, M., Lapidus, S., Bassiri, H., et al.	American College of Rheumatology Clinical Guidance for Multisystem Inflammatory Syndrome in Children Associated With SARS– CoV- 2 and Hyperinflammation in Pediatric COVID-19: Version 3	*Arthritis & Rheumatology / Clinical Practice Guideline*	• The American College of Rheumatology has released their updated guidance on the diagnosis and management of MIS-C associated with SARS-CoV-2. • Multiple case definitions for MIS-C were included to maintain a broad differential diagnosis. Common clinical features to watch out for include fever, mucocutaneous findings (rash, conjunctivitis, edema of the hands/feet, red/cracked lips, and strawberry tongue), myocardial dysfunction, cardiac conduction abnormalities, shock, gastrointestinal symptoms, and lymphadenopathy, and neurological symptoms. • Currently, there are no RCTs that evaluate different treatment regimens for MIS-C. Recommendations in the CPG were based on experience from managing MIS-C, nonrandomized cohort studies, and higher quality evidence from pediatric conditions with similar clinical presentations. • The first-line therapy in the treatment algorithm for MIS-C is dual therapy using intravenous immunoglobulin (IVIG) 2g/kg and Methylprednisolone IV 1-2mg/kg/day. The treatment of children with persistent fever or who present with ongoing and significant end-organ involvement should be intensified to higher dose Methylprednisolone IV 10-30mg/kg/day or high dose Anakinra, or Infliximab IV 5-10 mg/kg.

Evidence on Equipment & Devices

Date	Author/s	Title	Journal/ Article Type	Summary
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Evidence on Traditional Medicine

Date	Author/s	Title	Journal/ Article Type	Summary
-	-	-	-	-

Evidence on Preventive & Promotive Health

Evidence on Screening/Surveillance

Date	Author/s	Title	Journal/ Article Type	Summary
31 Jan 2022	Woloshin, S., Dewitt, B., Krishnamurti, T., and Fischhoff, B.	Assessing How Consumers Interpret and Act on Results From At-Home COVID-19 Self-test Kits: A Randomized Clinical Trial	*JAMA Network / Randomized clinical trial*	• Participants in the United States (n=360) were randomized to receive either FDA-authorized instructions (authorized), the intervention instructions (intervention), or no instructions (control), and to a scenario of either having a high pretest probability of infection (COVID-19 symptoms and/or a close contact with COVID-19) or low pretest probability (no symptoms and no contact). • Outcomes that were measured were the proportion of participants in the high pretest probability who chose to self-quarantine and the perceived probabilities of being infected after testing positive or negative using the at-home COVID-19 test kit. • Of the participants who had a positive test result, 95% (322 of 338; 95% CI, 0.92 to 0.97) chose to quarantine regardless of the instructions received. However, participants with a negative result who were in the high pretest probability cohort were more likely to fail to undergo self-quarantine when given the authorized instructions (33%) than with the intervention (14%; 95% CI for the 19% difference, 6% to 31%) or control (24%; 95% CI for the 9% difference, –4% to 23%). The authors recommended to redesign the test instructions that follow decision science principles to improve compliance and reduce the harms of self-administered test kits.

Evidence on Preventive & Promotive Health (continued)

Evidence on Personal Measures

Date	Author/s	Title	Journal/ Article Type	Summary
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Evidence on Community Measures

Date	Author/s	Title	Journal/ Article Type	Summary
01 Feb 2022	Montgomery, M., Hayter, A., Klu, J., and Pieper, U.	Global Analysis of Healthcare Waste in the Context of COVID-19: Status, Impacts, and Recommendations	WHO / Technical review	• Based on the latest available data of the WHO in 2019, 33% healthcare facilities globally do not safely manage healthcare waste. This number is magnified to up to 60% in the least developed countries. • In the context of COVID-19, approximately 87,000 tons (equivalent to 261,747 jumbo jet planes) of PPE units are expected to have ended up as waste. In addition, 140 million test kits, which have the potential to generate 2,600 tons of non-infectious waste and 731,000 liters of chemical waste. The administration of 8 billion doses of vaccines globally have produced 144,000 tons of additional waste (in needles, syringes, and safety collector boxes). • The WHO noted that while these materials are essential in the fight against the pandemic, improper waste management will impact the environment and the communities living near poorly managed landfills and waste disposal sites. • The report recommended environmentally sustainable practices in healthcare waste management such as the use of eco-friendly packaging and shipping, safe and reusable PPE, recyclable or biodegradable materials; investment in non-burn waste treatment technologies, and investments in the recycling sector.