Weekly Evidence Report

Health Technology Assessment Philippines

4 – 10 June 2022

Overview

The following report presents summaries of evidence the Department of Health (DOH) - Health Technology Assessment (HTA) Unit reviewed for the period of 4 -10 June 2022. The HTA Unit reviewed a total of 17 studies for the said period.

Evidence includes 2 studies on Epidemiology; 7 studies on Vaccines; 3 studies on Drugs; 0 studies on Transmission; 1 study on Equipment and Devices; 1 study on Medical and Surgical Procedures; 0 studies on Traditional Medicine; 2 studies on Preventive & Promotive Health; and 1 study on Other Health Technologies.

Sections

Evidence on Epidemiology

Local COVID-19 Case Tracker:

https://doh.gov.ph/2019-nCoV?gclid=CjwKCAjwjtOTBhAvEiwASG4bCOmLzFMQIjh8DX_VVSGA-HmO0Pt5_CscykID7xZv4zqlXG5vm9PM2xoC27QQAvD_BwE

Date	Author/s	Title	Journal/ Article Type	Summary
8 June 2022	WHO Global	Weekly epidemiological update on COVID-19 - 8 June 2022	*WHO Global Situation Report*	• Globally, the number of new weekly cases has continued to decline since a peak in January 2022. During the week of 30 May until 5 June 2022, over 3.023 million cases were reported, an 12% decrease as compared to the previous week. The number of new weekly deaths also continues to decline, with over 7 600 fatalities reported, representing a 22% decrease as compared to the previous week. • As of 5 June 2022, over 529 million confirmed cases and over six million deaths have been reported globally. • The Omicron VOC remains the dominant variant circulating globally, accounting for nearly all sequences reported. Among the Omicron sublineages, BA.2 and its descendent lineages (pooled lineages named BA.2.X) are declining but remain dominant, accounting for 44% and 19% respectively. Several variants with preliminary evidence of a growth advantage over other Omicron lineages show a global prevalence of <1% and are no longer rising, namely BA.2.11, BA.2.13, and BA.2.9.1 • Globally, three Omicron sublineages are rising in prevalence. BA.2.12.1 has reached a prevalence of 28%, BA.5 account for 4% and BA.4 for 2% of circulating variants. • Due to very low circulation among sequences submitted to GISAID in the last three months, Delta is now categorized by WHO as a 'previously circulating VOC,' in the same way that Alpha, Beta and Gamma are categorized. Importantly however, this does not imply that previously circulating VOCs cannot resurge in the future.
6 June 2022	New South Wales, COVID19 Critical Intelligence Unit	Post-acute sequelae of COVID-19 (long COVID)	*NSW/Rapid Review*	• Recent prevalence estimates suggest that between 3.69 and 20% of individuals who experience COVID-19 infection develop long COVID. • In a clinical setting, there is no definitive test for long COVID, and diagnosis is based on ruling out other similar conditions. • Risk factors for long COVID include: being female, being older, living in more deprived areas,working in social care, teaching and education or health care, and having another activity-limiting health condition or disability. (cont to next page)

Evidence on Epidemiology (cont.)

Date	Author/s	Title	Journal/ Article Type	Summary
6 June 2022	New South Wales, COVID19 Critical Intelligence Unit	Post-acute sequelae of COVID-19 (long COVID)	*NSW/Rapid Review*	(cont.) • Protective factors for long COVID include vaccination and young age. • Information on the effect of newer variants, such as Omicron, on long COVID is currently lacking. • Various models of care and clinical guidelines have been developed, however, the evidence-base for these is low quality and is evolving.

Evidence on Vaccines

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

WHO COVID-19 Vaccine Tracker:
https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines

WHO SAGE Vaccine Recommendations:
https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization

Local COVID-19 Vaccine Updates: https://doh.gov.ph/vaccines

Date	Author/s	Title	Journal/ Article Type	Summary
9 June 2022	Groot, G., et al.	What is known about hybrid immunity to COVID-19?	*Saskachewan Health Authority/Rapid Review*	• There is substantial immunologic and increasing epidemiologic evidence that vaccination following infection further increases protection against subsequent illness among those who have been previously infected. • Laboratory studies indicate that hybrid immunity (i.e., immunity conferred by the combination of previous infection and vaccination) offers greater protection against COVID-19 infection.
8 June 2022	Lewis, N., et al.	Effectiveness of the Ad26.COV2.S (Johnson & Johnson) COVID-19 Vaccine for Preventing COVID-19 Hospitalizations and Progression to High Disease Severity in the United States	*Clinical Infectious Diseases / case control analysis*	• In a multicenter case-control analysis of US adults (≥18 years) hospitalized March 11–December 15, 2021, VE against susceptibility to COVID-19 hospitalization (VEs), VE against disease progression (VEp) to death or invasive mechanical ventilation (IMV), was estimated. • After excluding patients receiving mRNA vaccines, among 3,979 COVID-19 case-patients (5% vaccinated with Ad26.COV2.S) and 2.229 controls (13% vaccinated with Ad26.COV2.S), VEs of Ad26.COV2.S against COVID-19 hospitalization was 70% (95% CI: 63%–75%) overall, including 55% (29%–72%) among immunocompromised patients, and 72% (64%–77%) among immunocompetent patients, for whom VEs was similar at 14–90 days (73% [59%–82%]), 91–180 days (71% [60%–80%]), and 181–274 days (70% [54%–81%]) post-vaccination. Among hospitalized COVID-19 case-patients, VEp was 46% (18%–65%) among immunocompetent patients.

Evidence on Vaccines (cont.)

Date	Author/s	Title	Journal/ Article Type	Summary
8 June 2022	Lin, D.Y., et al	Durability of Protection Against Symptomatic COVID-19 Among Participants of the mRNA-1273 SARS-CoV-2 Vaccine Trial	*JAMA Open Network/ cohort study*	• The study included 28 451 participants who tested negative for SARS-CoV-2 at baseline and had received 2 doses of vaccine by the end of the blinded phase. Participants received the first dose between July 27 and October 23, 2020. COVID-19 cases were defined by at least 2 systemic symptoms or at least 1 respiratory sign or symptom and were confirmed by a positive SARS-CoV-2 reverse transcriptase–polymerase chain reaction assay result. • A total of 14 164 patients with 769 cases of COVID-19 were in the placebo group, and 14 287 patients with 56 cases of COVID-19 were in the mRNA-1273 group. • The VE reached 92.6% (95% CI, 80.5%-97.2%) at 40 days after dose 1 and increased gradually to a peak of 94.1% (95% CI, 89.5%-96.7%) at 120 days. The VE started to decrease at approximately 120 days and dropped to 89.6% (95% CI, 41.7%-98.2%) at 200 days. The results show mild waning of VE over time and are more informative about duration of protection than previous estimates. The level of protection was still high even 200 days after dose 1, although there was considerable uncertainty in estimating VE near the end of blinded follow-up.
8 June 2022	Yechezkel, M., et al.	Safety of the fourth COVID-19 BNT162b2 mRNA (second booster) vaccine	*medRxiv / prospective observational study*	• A prospective observational study to compare the short-term effects of the first and second BNT162b2 mRNA COVID-19 vaccine booster doses. 2,019 participants received smartwatches and filled in a daily questionnaire on systemic reactions to the vaccine. • Substantial differences from the baseline were found 72 hours post vaccination in terms of both self-reported and physiological reactions. No significant differences in reactions was observed between the first and second boosters. It was also found that participants who experienced more severe reactions to the first booster tended to likewise experience more severe reactions to the second booster.
6 June 2022	Ritcherman, A., et al	Durability of SARS-CoV-2 mRNA Booster Vaccine Protection Against Omicron Among Health Care Workers with a Vaccine Mandate	*Clinical Infectious Diseases / test-negative case-control study*	• Benchmarked against Delta, vaccine effectiveness of two vaccine doses was lower during Omicron, with no significant protection against infection. Booster doses added significant protection, although they also showed reduced effectiveness during Omicron.

(continue to next page)

Evidence on Vaccines (cont.)

Date	Author/s	Title	Journal/ Article Type	Summary
6 June 2022	Ritcherman, A., et al	Durability of SARS-CoV-2 mRNA Booster Vaccine Protection Against Omicron Among Health Care Workers with a Vaccine Mandate	*Clinical Infectious Diseases / test-negative case-control study*	(cont.) • Compared to employees who had received two vaccine doses, three BNT162b2 doses had a relative effectiveness of 50% (95% CI 42-56%) during Omicron, relative to 78% (95% CI 63-87%) during Delta; three mRNA1273 doses had a relative effectiveness of 56% (95% CI 45-65%) during Omicron, relative to 96% (95% CI 82-99%) during Delta. Restricting the sample to symptomatic tests yielded similar results to the primary analysis. After initial waning in BNT162b2 booster protection against infection, it remained largely stable for at least 16 weeks after vaccination.
6 June 2022	Hulme W., et al	Effectiveness of BNT162b2 booster doses in England: an observational study in OpenSAFELY -TPP	*medRxiv/ observational cohort study*	• Observational cohort study used data from OpenSAFELY-TPP database,to estimate the effectiveness of boosting with BNT162b2 compared with no boosting in eligible adults who had received two primary course vaccine doses between 16 September and 16 December 2021 when the Delta variant of SARS-CoV-2 was dominant. • Among 4,352,417 BNT162b2 booster recipients matched with unboosted controls,estimated effectiveness of a booster dose compared with two doses only was 50.7% (95%CI 50.1-51.3) for positive SARS-CoV-2 test, 80.1% (78.3-81.8) for COVID-19 hospitalisation,88.5% (85.0-91.1) for COVID-19 death, and 80.3% (79.0-81.5) for non-COVID-19 death. • Estimated effectiveness was similar among those who had received a BNT162b2 or ChAdOx1-S two-dose primary vaccination course, but effectiveness against severe COVID19 was slightly lower in those classified as clinically extremely vulnerable (76.3% (73.1- 79.1) for COVID-19 hospitalisation, and 85.1% (79.6-89.1) for COVID-19 death). Estimated effectiveness against each outcome was lower in those aged 18-65 years than in those aged 65 and over

Evidence on Vaccines (cont.)

Date	Author/s	Title	Journal/ Article Type	Summary
6 June 2022	Washrawirul et al..	Global prevalence and clinical manifestations of cutaneous adverse reactions following COVID-19 vaccination: A systematic review and meta-analysis	*PubMed/Systematic Review-Meta Analysis*	• A total of 300 studies were included in a systematic review of which 32 studies with 946,366 participants were included in the meta-analysis. • The pooled prevalence of cutaneous manifestations following COVID-19 vaccination was 3.8% (95% CI, 2.7%-5.3%). COVID-19 vaccines based on the mRNA platform had a higher prevalence than other platforms at 6.9% (95% CI, 3.8%-12.3%). • Various cutaneous manifestations have been reported from injection site reactions which were the most common (72.16%) to uncommon adverse reactions such as delayed inflammatory reactions to tissue filler (0.07%) and flares of pre-existing dermatoses (0.07%). • Severe cutaneous reactions such as anaphylaxis have also been reported, but in rare cases (0.05%). • Cutaneous adverse reactions are common, especially in those receiving mRNA vaccines. Most reactions are mild and are not contraindications to subsequent vaccination except for anaphylaxis, which rarely occurs. • COVID-19 vaccination may also be associated with flares of pre-existing dermatoses and delayed inflammatory reactions to tissue filler. Patients with a history of allergies, pre-existing skin conditions, or scheduled for filler injections should receive additional pre-counseling and monitoring.

Evidence on Drugs

Date	Author/s	Title	Journal/ Article Type	Summary
9 June 2022	Levin, M., , et al.	Intramuscular AZD7442 (Tixagevimab-Cilgavimab) for Prevention of Covid-19	*PubMed / Phase 3 Randomized Control Trial*	• In an ongoing phase 3 trial,participants were randomly assigned in a 2:1 ratio to receive a single dose (two consecutive intramuscular injections, one containing tixagevimab and the other containing cilgavimab) of either 300 mg of AZD7442 or saline placebo, and they were followed for up to 183 days in the primary analysis. The primary safety end point was the incidence of adverse events after a single dose of AZD7442. The primary efficacy end point was symptomatic Covid-19 (SARS-CoV-2 infection confirmed by means of reverse-transcriptase-polymerase-chain-reaction assay) occurring after administration of AZD7442 or placebo and on or before day 183 (continue next page)

Evidence on Drugs (cont.)

Date	Author/s	Title	Journal/ Article Type	Summary
9 June 2022	Levin, M., , et al.	Intramuscular AZD7442 (Tixagevimab-Cilgavimab) for Prevention of Covid-19	*PubMed / Phase 3 Randomized Control Trial*	(cont.) • In total, 1221 of 3461 participants (35.3%) in the AZD7442 group and 593 of 1736 participants (34.2%) in the placebo group reported having at least one adverse event, most of which were mild or moderate in severity. Symptomatic Covid-19 occurred in 8 of 3441 participants (0.2%) in the AZD7442 group and in 17 of 1731 participants (1.0%) in the placebo group (relative risk reduction, 76.7%; 95% confidence interval [CI], 46.0 to 90.0; P<0.001); extended follow-up at a median of 6 months showed a relative risk reduction of 82.8% (95% CI, 65.8 to 91.4). Five cases of severe or critical Covid-19 and two Covid-19-related deaths occurred, all in the placebo group.
8 June 2022	Sirijatuphat, R., et al	Early Treatment of Favipiravir in COVID-19 Patients Without Pneumonia: A Multicentre, Open-Labelled , Randomized Control Study	*medRxiv/ randomized, prospective study*	• PCR-confirmed SARS-CoV-2-infected patients without pneumonia were enrolled (2:1) within 10 days of symptomatic onset into FPV and control arms. The former received 1800 mg FPV twice-daily (BID) on Day 1 and 800 mg BID 5-14 days thereafter until negative viral detection, while the latter received supportive care only. The primary endpoint was time to clinical improvement, which was defined by a reduced National Early Warning Score (NEWS) or score of <1. • The median time to sustained clinical improvement by (NEWS) was 2 vs 14 days for FPV and control arms respectively (adjusted hazard ratio (aHR) of 2.77, 95% CI 1.57-4.88, P <0.001). • The FPV arm also had significantly higher likelihoods of clinical improvement within 14 days after enrolment by NEWS (79% vs 32% respectively, P <0.001), particularly female patients (aOR 6.35, 95% CI 1.49-27.07, P <0.001). 8 (12.9%) and 7 (22.6%) patients in FPV and control arms developed mild pneumonia at a median (range) 6.5 (1-13) and 7 (1-13) days after treatment, respectively (P = 0.316); all recovered well without complications.

Evidence on Drugs (cont.)

Date	Author/s	Title	Journal/ Article Type	Summary
6 June 2022	Batista, D., et al.	Use of anticoagulants in patients with COVID-19: a living systematic review and meta-analysis	*Pubmed / Systematic Review and Meta-analysis*	• A total of 401 studies were initially selected. Of those, 9 met the inclusion criteria and were therefore analyzed (a total of 6,004 patients being analyzed). • In non-hospitalized COVID-19 patients, no significant difference was found between post-discharge prophylactic anticoagulation and no intervention regarding venous thromboembolism or bleeding at 30 days. In hospitalized COVID-19 patients, full anticoagulation resulted in a slight reduction in thrombotic events at 30 days (risk difference, -0.03; 95% CI, -0.06 to -0.00; p = 0.04; I2 = 78%), the quality of evidence being moderate. However, no significant difference was found between full anticoagulation and no intervention regarding the risk of major bleeding, the quality of evidence being very low. No significant difference was found between intermediate- and standard-dose prophylactic anticoagulation (risk difference, -0.01; 95% CI, -0.07 to 0.06; p = 0.81; I2 = 0%), the quality of evidence being very low. • Therapeutic anticoagulation appears to have no effect on mortality in COVID-19 patients, resulting in a slight reduction in venous thromboembolism in hospitalized patients.

Evidence on Transmission

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

Evidence on Equipment and Devices

Date	Author/s	Title	Journal/ Article Type	Summary
6 June 2022	Dewald, F., et al.	Effective high-throughput RT-qPCR screening for SARS-CoV-2 infections in children	*medRxiv/ prospective validation study*	• This is a prospective validation study for a high-throughput approach (Lolli-Method) developed for SARS-CoV-2 detection in children, combining non-invasive sample collection with an RT-qPCR-pool testing strategy. SARS-CoV-2 infections were diagnosed with sensitivities of 100% and 93.9% when viral loads were >10E6 copies/ml and >10E3 copies/ml in corresponding Naso-/Oropharyngeal-swabs, respectively.. (continue to next page)

Evidence on Equipment and Devices

Date	Author/s	Title	Journal/ Article Type	Summary
6 June 2022	Dewald, F., et al.	Effective high-throughput RT-qPCR screening for SARS-CoV-2 infections in children	*medRxiv/ prospective validation study*	(cont.) • For effective application of the Lolli-Method in schools and daycare facilities, SEIR-modeling indicated a preferred frequency of two tests per week. The developed test strategy was implemented in 3,700 schools and 698 daycare facilities in Germany, screening over 800,000 individuals twice per week • In a period of 3 months, 6,364 pool-RT-qPCRs tested positive (0.64%), ranging from 0.05% to 2.61% per week. Notably, infections correlated with local SARS-CoV-2 incidences and with a school social deprivation index. Moreover, in comparison with the alpha variant, statistical modeling revealed a 36.8% increase for multiple (≥2 children) infections per class following infections with the delta variant. The Lolli-Method is a powerful tool for SARS-CoV-2 surveillance and infection control in schools and daycare.

Evidence on Medical and Surgical Procedures

Date	Author/s	Title	Journal/ Article Type	Summary
7 June 2022	Czeresnia J., et al.	Transplantation of solid organs recovered from deceased donors recently infected by SARS-CoV-2 in the United States	*medRxiv/ Case Series Review*	• The COVID-19 pandemic has reduced access to solid organ transplantation, compounding organ shortages and waitlist mortality. A continued area of uncertainty is the safety of transplanting organs recovered from SARS-CoV-2 infected donors, as autopsies of patients who died with COVID-19 show that the virus can be found in extra-pulmonary organs. This review based on national transplant database for recipients of organs recovered from donors recently infected by SARS-CoV-2. • Cases were defined as adult (≥ 18 years) recipients of organs recovered from deceased donors who tested positive for SARS-CoV-2 by nasopharyngeal or lower respiratory sample polymerase chain reaction or antigen assay within 7 days of organ transplantation. (continue to next page)

Evidence on Medical and Surgical Procedures

Date	Author/s	Title	Journal/ Article Type	Summary
7 June 2022	Czeresnia J., et al.	Transplantation of solid organs recovered from deceased donors recently infected by SARS-CoV-2 in the United States	*medRxiv/ Case Series Review*	(cont.) • For kidney, liver, and heart transplants, Kaplan-Meier curves of both overall and graft survival at 90 days were similar between cases and controls. Data shows that transplanting kidneys, livers, and hearts recovered from deceased donors recently infected by SARS-CoV-2 was not associated with increased recipient mortality or worse graft-survival. Prospective studies are needed to confirm our findings and provide insights on optimal post-transplant management of these recipients.

Evidence on Traditional Medicine

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

Evidence on Preventive & Promotive Health

Evidence on Screening

Date	Author/s	Title	Journal/ Article Type	Summary
9 June 2022	Groot, G., et al	What is the evidence around testing for asymptomatic COVID on the day of surgery?	*Saskachewan Health Authority/Rapid Review*	• Current requirements for preoperative COVID-19 testing are highly variable across jurisdictions, with some requiring preoperative testing for all patients 24-72 hours prior to surgery and some not recommending testing of asymptomatic patients at all • Studies describing low rates of asymptomatic positivity are limited to early in the pandemic, prior to the widespread availability of vaccines and the emergence of variant strains. These studies show very low rates of asymptomatic positives when testing within 72 hours of surgery • Mixed evidence on safety of surgery in asymptomatic COVID-19 infected patients • Preliminary evidence indicates that it may be safe to discontinue asymptomatic preoperative testing, but there are too many unknowns that have not yet been addressed with regards to the impact of vaccination status and the altered pathophysiology associated with currently circulating variants

Evidence on Preventive & Promotive Health (cont)

Evidence on Screening

Date	Author/s	Title	Journal/ Article Type	Summary

6 June 2022	Burns, J. et al.	International travel- related control measures to contain the COVID- 19 pandemic: a rapid review	*Cochrane Library/Rapid Review*	• Overall 62 studies were included in the analysis, (49 modelling studies;13 observational) covering variety of settings and levels of community transmission.
				• With much of the evidence derived from modelling studies, notably for travel restrictions reducing or stopping cross- border travel and quarantine of travellers, there is a lack of 'real- world' evidence.
				• The certainty of the evidence for most travel- related control measures and outcomes is very low and the true effects are likely to be substantially different from those reported.
				• Broadly, travel restrictions may limit the spread of disease across national borders.
				  ○ Symptom/exposure- based screening measures at borders on their own are likely not effective;
				  ○ PCR testing at borders as a screening measure likely detects more cases than symptom/exposure- based screening at borders, although if performed only upon arrival this will likely also miss a meaningful proportion of cases.
				  ○ Quarantine, based on a sufficiently long quarantine period and high compliance is likely to largely avoid further transmission from travellers
				  ○ Combining quarantine with PCR testing at borders will likely improve effectiveness.
				  ○ Many studies suggest that effects depend on factors, such as levels of community transmission, travel volumes and duration, other public health measures in place, and the exact specification and timing of the measure.
				• Future research should be better reported, employ a range of designs beyond modelling and assess potential benefits and harms of the travel- related control measures from a societal perspective.

Evidence on Preventive & Promotive Health

Evidence on Personal Measures

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

Evidence on Community Measures

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

Evidence on Other Health Technologies

Date	Author/s	Title	Journal/ Article Type	Summary
6 June 2022	Bezerra, G., et al.	Telemedicine Application and Assessment During the COVID-19 Pandemic	*PubMed/ Systematic Review*	• The present study is a systematic review of studies that had applied telemedicine during the COVID-19 pandemic and had assessed its effects on the delivered care. A 1-year period was covered in order to assess the initiatives developed during the pandemic time and that had already evaluated the effects of the telemedicine program that had been implemented. All the analyzed studies evidenced a positive effect of telemedicine in the treatment of different conditions, including chronic diseases, mental disorders and oncologic diseases.