INTRODUCTION

On April 1st 2022, Malaysia announced an endemic phase to the coronavirus disease 2019 (COVID-19). Following the endemic stage, requirements for home isolation, mask mandate and social distancing became less stringent. Individuals were free to enter business premises regardless of their vaccination statuses. By then, 98% of the adult population had received their complete doses [1]. Nevertheless, the Ministry of Health (MoH) Malaysia was not complacent about COVID-19. The ministry was constantly updating the public on new cases, SARS-CoV-2 variants, and imparting information on the importance of preventing serious infections arising from COVID-19 variants of concern (VoC) and variants being monitored (VBM). The development of efficacious SARS-CoV-2 vaccines and adequate immunogenicity was acknowledged as crucial to preventing the spread of VoC and having protective mechanisms against the more infectious strains. Viruses like SARS-CoV-2 continue to evolve as changes in the genetic code induced by genetic mutations or viral recombination occur during replication of the genome. A lineage is a collection of genetically distinct viral strains that have a common ancestor. A variety of the SARS-CoV-2 viruses has one or more mutations that set it apart from other variants. Recombinant refers to combining genetic material from two separate variants to form a new variant. Several SARS-CoV-2 variants have been identified throughout this pandemic in the United States and all over the world, as was to be expected. Scientists evaluated the genetic differences between viruses to find variants, including recombinants, and how they were related to one another to inform local outbreak investigations and comprehend national trends.
COVID-19 Booster Vaccination in Malaysia

Even after vaccination, individuals were at risk of contracting SARS-CoV-2 due to waning immunity with time and the emergence of different SARS-CoV-2 variants such as Alpha (B.1.1.7 and Q lineages), Beta (B.1.351 and descendent lineages), Gamma (P.1 and descendent lineages) and Delta (B.1.617.2 and AY lineages). Current vaccines are effective at preventing severe diseases, hospitalisation, and death due to COVID-19, yet cannot protect against an infection. Immunological studies have documented a gradual decline in antibody levels in vaccinated individuals. After the initial vaccination series, a booster dose is necessary to maintain antibody levels to prevent the spread of the more infectious SARS-CoV-2 variants [2-4]. A previous study of COVID-19 vaccine boosters demonstrated immunological benefits, and their side-effect profiles following vaccination were deemed mild and acceptable [5]. This article provides a summary of the evidence with policy recommendations for booster doses of COVID-19 vaccination.

MATERIALS AND METHODS

Data were collected following a comprehensive search strategy using online databases. The data was extracted from the following databases: Science Direct, Scopus, and EBSCO: MEDLINE. The search was carried out using relevant keywords that were directly linked with the topic of interest with various synonyms. The search was restricted to the English language and published literature was searched between January 2022 to July 2023. The two Boolean operators OR and AND were used, for example, “coronavirus disease 2019 * COVID-19 * AND (OR Vaccination* Immunization)” AND “(Malaysia*)” AND “(Booster* OR Fourth doses). In addition, for the search to be comprehensive, policy statements OR guidelines on vaccination in Malaysia, e.g. press statements of the MoH, Senior Defence Minister, Ministers, and press conferences of the MoH, Director General of Health, the MoH's website, Director General of Health's Facebook, Telegrams of both the Crisis Preparedness and Response Centre of MOH and the National Security Council (MKN). Manual searching of bibliographies was carried out to retrieve other relevant studies. Full texts and metadata were imported to the Zotero program to assist with data collection and to remove duplicates.

Findings were synthesised and presented in recurring themes.

RESULTS

History

Malaysia launched its COVID-19 vaccination program at the beginning of March 2021, when the country reported more than 3.7 million confirmed cases and 1,255 deaths, making it one of the most affected nations in the Western Pacific region [6]. As of 10th March 2022, Malaysia had administered at least 68 million doses of the COVID-19 vaccines, with over 27 million people having received at least one dose, 25 million having completed two doses, and 15 million have received a booster dose [7]. The National COVID-19 Immunisation Programme, also known as NIP or PICK, was a national vaccination campaign that was implemented by the Malaysian government as a strategy for bringing to a halt the spread of coronavirus disease 2019 (COVID-19) [7]. To facilitate access, widen coverage, and accelerate vaccination rates, the MOH partnered with ProtectHealth Corporation Sdn. Bhd. (ProtectHealth) to expedite private medical practitioners and healthcare non-governmental organisations’ (NGOs) participation and support of PICK. Through the public-private healthcare partnership, PROTECTHEALTH, innovations in public-private engagements were introduced, including the setting up of vaccine delivery centres at private clinics (PPVGP), private hospitals (PPVHS), and ambulatory care centres (PPVACC) as well as specialist clinics (PPVKP) [8].

Voluntary access to the AstraZeneca vaccine in the earlier phase of the vaccination program resulted in large vaccination centres being established in the Klang Valley, which were later expanded to Johor, Penang, and Sarawak. The introduction of the integrated vaccination centres (PPV Integrasi) witnessed facilities delivering up to 15,000 doses daily [9].

PICK was tasked to ensuring equitable vaccine access. To achieve inclusivity and fulfil the vaccination needs of the underprivileged, migrant populations, and those living in rural and remote communities, programmes such as Program Mobilisasi Vaksin Komuniti (MOVAK) were introduced in the community and industry settings. Health-related non-
governmental organisations ensured that the disabled communities were not left behind and could access vaccines. Malaysia attained several awards including being in the top ten of the highest rates for having a fully vaccinated population against COVID-19 globally. In addition, PROTECTHEALTH was hailed as the public-private healthcare partnership of the year – Malaysia at the Healthcare Asia Awards 2022 [9, 10].

Following the World Health Organization’s statement on 1 May 2023 that COVID-19 was no longer a Public Health Emergency of International Concern (PHEIC), the MoH of Malaysia announced revised protocols with regards to facemask usage and a shortening of the home isolation period from seven to five days [11]. These measures took effect from 5 July 2023. While protocols to contain the spread of the Covid-19 virus have been relaxed, nevertheless, exercising self-precaution and vigilance were advocated to reduce the number of infections.

Roll-out of COVID-19 vaccine booster doses

Hospitalisation and mortality rates related to COVID-19 have decreased in Malaysia with high vaccination rates among priority groups [12]. When social restrictions were relaxed, this resulted in a fleeting rise in community infection rates. The concurrent rise in rates of severe comorbid conditions and mortality were nevertheless significantly less prominent. It is thought that protection against COVID-19 infections declines rapidly with time since the last vaccination, while effectiveness against the severe disease remains relatively stable. As effectiveness declines, older adults and people with comorbidities continue to be at the greatest risks for morbidity and mortality. This is amalgamated by the emergence of future variants; even a modest reduction in vaccine effectiveness in such vulnerable individuals will result in an increase in severe respiratory-related illnesses, hospitalisation and death [13].

The program for booster dose administration, also known as PICK-B, began in Malaysia on October 13, 2021, for those who had received complete vaccination of the primary series. The program was expected to benefit 23 million Malaysians.

The COVID-19 booster shots were not compulsory, however, were provided free of charge to all Malaysians, including to citizens and non-citizens [14]. The recipients need not register to be eligible for booster doses. The MySejahtera application will automatically send notifications about the appointment based on the last dose. MySejahtera is a mobile application developed by Entomo Malaysia and the Government of Malaysia to manage the COVID-19 outbreak in Malaysia. It can be used to conduct contact tracing, self-quarantine, and book or reschedule COVID-19 vaccination appointments [15]. Following waves of rising infections, as of 10th February 2022, 98% of the country’s adult population eligible for vaccination had completed the required doses and were successfully inoculated, while 53.9% had received their booster shots. The plan to vaccinate adolescents and toddlers as young as 5, and other special interest population groups was also rolled out in phases across the country depending on vaccine manufacturers’ supplies and deliverables [16]. Table 1 depicts the recommendation for COVID-19 booster type [17]. Table 2 depicts the groups recommended to receive booster doses [18].

<table>
<thead>
<tr>
<th>Primary Series</th>
<th>*Recommended Booster</th>
<th>Eligibility After Completion of Primary Series</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer</td>
<td>Pfizer or AstraZeneca</td>
<td>At least 3 months</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>Pfizer or AstraZeneca</td>
<td></td>
</tr>
<tr>
<td>Sinovac</td>
<td>Pfizer, AstraZeneca or Sinovac</td>
<td></td>
</tr>
<tr>
<td>Sinopharm</td>
<td>Pfizer or AstraZeneca</td>
<td></td>
</tr>
<tr>
<td>Moderna</td>
<td>Pfizer or AstraZeneca</td>
<td></td>
</tr>
<tr>
<td>CanSinoBio</td>
<td>Pfizer or AstraZeneca</td>
<td></td>
</tr>
<tr>
<td>Sputnik V</td>
<td>Pfizer or AstraZeneca</td>
<td></td>
</tr>
<tr>
<td>Janssen</td>
<td>Pfizer or AstraZeneca</td>
<td>At least 2 months</td>
</tr>
</tbody>
</table>

*If a recipient has a medical contraindication that makes them unsuitable for the mRNA vaccine, they will be advised accordingly and be offered another alternative vaccine
Table 2 Recommendation for groups to receive COVID-19 booster

<table>
<thead>
<tr>
<th>Recommended groups for booster doses</th>
<th>Older age groups/ patients at any age with any of the condition below:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Older persons</td>
<td>Geriatrics aged ≥60 years</td>
</tr>
<tr>
<td>Persons with moderately and severely immunocompromising conditions</td>
<td>i. Active cancer</td>
</tr>
<tr>
<td></td>
<td>ii. Transplant recipients</td>
</tr>
<tr>
<td></td>
<td>iii. Immunodeficient</td>
</tr>
<tr>
<td></td>
<td>iv. People living with *HIV</td>
</tr>
<tr>
<td></td>
<td>v. Patients on immunosuppressants</td>
</tr>
<tr>
<td>Adults with comorbidities that put them at higher risks for severe diseases</td>
<td>Diabetes, hypertension, chronic cardiac, lung and kidney diseases, and neurodegenerative diseases are associated with higher risks for severe diseases</td>
</tr>
<tr>
<td>Vulnerable population</td>
<td>Pregnant women and healthcare workers</td>
</tr>
</tbody>
</table>

*HIV= human immunodeficiency virus

DISCUSSION

The Rationale for Booster Doses

Booster doses given after the completion of the primary series is meant to revive and strengthen an immune response that has weakened since last vaccination. Vaccines containing either the ancestral strain or vaccines incorporating a variant strain may be used for booster doses (first and/or second and subsequent boosters). For vaccines of two-dose primary series, the first and second booster doses will be the third and fourth shots while for vaccines of single-dose primary series, the first and second booster doses will be the second and third shots. The rationale for the booster shots is to restore immunity and with a heterologous combination, it could possibly enhance protection. In some countries, second and third booster doses are currently being offered complimentary (i.e. fourth doses to older adults and fifth doses to immunocompromised persons) [19], [20], [21].

Recommended groups for booster doses

Malaysia, in accordance to the World Health Organization's recommendation considered booster shots for the following group to reduce the risks for severe comorbid conditions, mortality, and disruption to the utilisation of healthcare services.

i) Older persons (geriatric aged ≥60 years old)

As of 15th July 2022, of the 2.57 million senior citizens who had taken their first booster shots, only 93,496 (3.63%) proceeded to get their second booster dose in Malaysia [21]. In comparison to unvaccinated individuals, the overall COVID-19 vaccine efficacy within 5 months of completing the primary vaccination cycle was significantly high in the geriatric population, associated with an 80% lower risk of SARS-CoV-2 infection, an 86% lower risk of COVID-19 hospitalisation and ICU admission, and an 88% lower risk of death. The efficacy against the risk of SARS-CoV-2 infection, COVID-19 hospitalisation, ICU admission, and mortality was 70%, 83%, 86%, and
88%, respectively, after 5 months. A previous study had shown that those who received vaccine booster doses had a 75% lower risk of SARS-CoV-2 infections and between 81 and 83% lower risk of COVID-19 hospitalisation, ICU admission, and death, respectively, compared to those who had completed the COVID-19 vaccination cycle for more than 5 months. The administration of COVID-19 vaccine boosters resulted in greater protection (i.e., between 63 and 87%) against these same endpoints compared to individuals who completed a primary COVID-19 vaccination cycle early (i.e., within 5 months) [22]. Therefore, it is recommended that COVID-19 vaccine booster doses are immediately available to the elderly, who experience a more rapid decline in post-vaccination immunity and protection and who are also more susceptible to SARS-CoV-2 complications.

**ii) All persons with moderately and severely immunocompromising conditions**

For individuals with immunocompromised conditions, the initial vaccination may not produce enough protective immunoglobulins to quickly act upon an infection [23]. In these instances, individuals may require an additional COVID-19 vaccine dose to sustain the protection. People aged 5 and older who are moderately to severely immunocompromised may be eligible for an additional dose. Moderately and severely immunocompromised individuals include those with:

a. Active cancer (active immunosuppressive treatment for solid tumour or haematological malignancy (including leukaemia, lymphoma, and myeloma) or within 12 months of cessation of such treatment.

b. Transplant recipients (those who have received a solid organ transplant and are receiving immunosuppressive therapy; those who have received a stem cell transplant) (within 2 years of transplantation, or taking immunosuppressive therapy)

c. Immunodeficiency (severe primary immunodeficiency, chronic dialysis)

d. People living with HIV with a current CD4+ differentiation cell count of 200 cells/L, have opportunistic infections, not on HIV treatment, and/or with a detectable viral load (i.e. advanced HIV disease/ acquired immunodeficiency syndrome (AIDS))

e. Those on immunosuppressants (active treatment that causes significant immunosuppression, such as high-dose corticosteroids, alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents, tumor-necrosis factor (TNF) blockers, or other highly immunosuppressive drugs; immunosuppressive chemotherapy or radiotherapy within the previous 6 months).

The shot for an immunocompromised person is typically administered 28 days after the second dose [22].

**iii) Adults with comorbidities that put them at higher risk for severe diseases**

Comorbidities that increase the risk of severe disease and death due to COVID-19 include diseases such as diabetes, hypertension, chronic cardiac, lung and kidney diseases, neurodegenerative diseases, and conditions associated with immunosuppression that are associated with a higher risk for severe diseases etc [24]. Individuals with comorbidities have reduced immunological responses to infection or immunisation, which may necessitate higher vaccine dosages or additional booster vaccines. According to a number of studies, individuals with comorbidities have an increased risk of developing severe COVID-19 and subsequent death [18, 25]. Previous studies have confirmed that individuals older than 16 with comorbidities who received a second booster dose had a lower risk of infection and developing respiratory-related illnesses than those who did not receive a booster dose. Furthermore, other studies have found that people with comorbidities such as Type 2 diabetes, cancer, end-stage renal disease, and other immunocompromising conditions had lower levels of SARS-CoV-2 antibody titers after vaccination when compared to healthy people [19],[24]. Thus, individuals who fall into this high-risk category may benefit from a booster vaccination.
iv) Pregnant women

Vaccination during pregnancy stimulates the production of antibodies that can protect the mother and the baby. When pregnant women receive an mRNA COVID-19 vaccine, their bodies produce antibodies against COVID-19, similar to non-pregnant individuals. Antibodies produced after pregnant women receive their mRNA COVID-19 vaccine were discovered in their baby's umbilical cord. This indicated that COVID-19 vaccination during pregnancy can help protect babies from COVID-19 via vertical transmission i.e. by transferring antibodies from the mother to the child [26]. Another study discovered that receiving a booster dose of an mRNA COVID-19 vaccine during pregnancy significantly increased the levels of antibodies found in the blood extracted within an umbilical cord. It thus indicates that receiving a COVID-19 booster vaccine during pregnancy can provide additional protection against COVID-19 [27].

v) Healthcare workers

Healthcare professionals are strongly encouraged to receive their COVID-19 booster shots to protect themselves in the event of a recurring pandemic that could cause the collapse of the national healthcare system. The Director General of Health expected an increase of 3,700 daily admissions to intensive care unit wards since December 2022 [28]. As a result of the increase in transmission rates in the country and influx of patients in healthcare centres, a significant number of COVID-19 infections circulated among healthcare workers, causing them to take sick or quarantine leave. This had placed the healthcare system in many states (constituencies) in a critical state. Services affected included ambulatory facilities, and there was also a shortage of ICU ward staff. As a result, medical personnel in Malaysia were strongly encouraged to receive a booster shot to prevent them from contracting severe COVID-19 infections, which could have further impacted the healthcare system.

Covid-19 Booster Vaccine Recommendation

Depending on the type of primary dose administered, the interval between a 2-dose primary series and a booster dose varies. Vaccines used for booster doses include Pfizer-BioNTech, Sinovac, and AstraZeneca. According to the Technical Working Task Force and the Director General of Health's circular No.1/2022, booster doses can be given with the same type (homologous) or a different type (heterologous) [29]. Regardless of the date, the interval is measured in calendar months. For Sinovac patients, booster dose was recommended after three months of the second dose. For patients who first received AstraZeneca and Pfizer-BioNTech, booster doses were recommended after three months of the second dose. If an mRNA vaccine is medically contraindicated, the recipient will have been offered another vaccine alternative based on medical advice [30].

The "COVID-19 vaccine effectiveness assessment in Chile" study, which was released by the Chilean government at a World Health Organization (WHO) consultation on October 25, 2021, revealed that the combination of the Sinovac vaccine with either Pfizer-BioNTech or AstraZeneca as the booster dose increased vaccine efficacy [31].

CONCLUSION

COVID-19 booster vaccination was recommended as a priority for pregnant women, healthcare workers, people with comorbid conditions, those immunosuppressed, and the elderly because of their distinctive circumstances. This information is useful for future vaccination policy and decision-making by policymakers and healthcare providers, particularly for including COVID-19 vaccination in national immunization strategies.

Conflict of interest

Authors declare none.

Acknowledgements

We wish to thank the Faculty of Pharmacy, UiTM for its continued support.

Authors’ Contribution

Conceptualization, NEAH and MLF; Methods, NEAH and MLF; Writing—original draft preparation, MLF and NFLM; Writing—review and editing, MLF and AOY

Funding

None.
Data Availability Statement

All relevant data are available in the article.

REFERENCES


