

Discussion | We demonstrated that SARS-CoV-2-specific IgA in human milk was present more frequently after vaccination with an mRNA-based vaccine compared with a vector-based vaccine. Additionally, IgG was present in all participants after receiving 2 vaccine doses, independent of vaccine type. However, IgG was detectable earlier after vaccination with either of the mRNA vaccines, which can be explained by timing of the second dose. A limitation of this study is that we did not measure neutralizing capacity of the human milk antibodies.

The most abundant antibody in human milk is IgA, which plays a key role in the first line of defense against invading viruses.⁵ Although, to our knowledge, no studies have shown indisputable evidence that human-milk IgA directly protects against respiratory tract infections, it is very likely that this antibody plays a critical role. Based on these data, we suggest that an mRNA-based vaccine is the optimal choice for lactating women when they want to transfer antibodies to their infants.

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Myocarditis Following COVID-19 BNT162b2 Vaccination Among Adolescents in Hong Kong

Cases of myocarditis following the second dose of messenger RNA (mRNA) vaccine are accruing worldwide, especially in younger male adults and adolescents.¹⁻⁴ In weighing the risk of myocarditis against the benefit of preventing severe COVID-19, Norway, the UK, and Taiwan have suspended the second dose of mRNA vaccine for adolescents. Similarly, adolescents (aged 12-17 years) in Hong Kong have been recommended to receive 1 dose of BNT162b2 instead of 2 doses 21 days apart since September 15, 2021 (Figure).

Methods | This cohort study was conducted before the arrival of the Omicron variant. We linked vaccination records with the Hong Kong territorywide electronic health record database through government-commissioned population-based COVID-19 vaccine safety surveillance.³ Among adolescents who received at least 1 dose of BNT162b2 between March 10 and October 18, 2021, inpatient myocarditis cases were identified using the *International Classification of Diseases, Ninth Revision, Clinical Modification* (422.x and 429.0). Adolescents with a history of myocarditis were excluded. The study was approved by the institutional review board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster and the Department of Health Ethics Committee with a waiver of informed consent because anonymized data were used. The statistical tests are described in the eMethods in the Supplement. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Results | A total of 224 560 first doses and 162 518 second doses of BNT162b2 were administered to adolescents. Forty-three adolescents had myocarditis-related hospitalization following receipt of BNT162b2 vaccination, and 84% of the hospitalizations (36 of 43) occurred after the second dose. The incidence rate was 3.12 (95% CI, 1.25-6.42) and 22.15 (95% CI, 15.51-30.67) per 100 000 persons for the first and second dose, respectively (Table). The number needed to harm for the first and second dose were 32 051 and 4515, respectively. The crude risk ratio of the second dose vs first dose was 7.11 (95% CI, 3.16-15.97). The cumulative incidence of myocarditis decreased from 43 cases in 202 315 adolescents vaccinated (21.25, 95% CI, 15.38-

Figure. Timeline of BNT162b2 Vaccination Policy Among Adolescents in Hong Kong

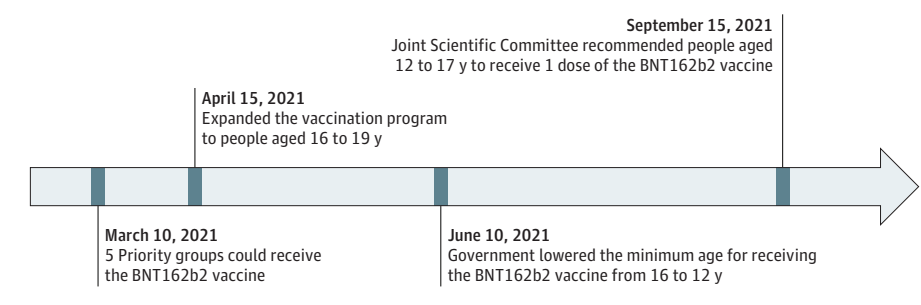


Table. Myocarditis Cases Following the BNT162b2 Vaccination Among 43 Adolescents in Hong Kong Before and After the Single-Dose Policy

| Variable | Male (n = 38 [88%]) | Female (n = 5 [12%]) | Total (n = 43 [100%]) |
|---|----------------------|----------------------------|------------------------|
| Age, mean (SD), y | 14.95 (1.35) | 14.20 (2.17) | 14.86 (1.46) |
| Before single-dose recommendation | | | |
| Cases, No. | 38 | 5 | 43 |
| Doses administered, total No. | 181 392 | 177 405 | 358 797 |
| Adolescents who received vaccination, total No. | 102 242 | 100 073 | 202 315 |
| After single-dose recommendation | | | |
| Cases, No. | 0 | 0 | 0 |
| Doses administered, total No. | 14 386 | 13 895 | 28 281 |
| Adolescents who received vaccination, total No. | 11 525 | 10 720 | 22 245 |
| Overall observational period | | | |
| Cases after first dose, No./recipients of first dose, total No. | 6/113 767 | 1/110 793 | 7/224 560 |
| Incidence after first dose per 100 000 persons (95% CI) | 5.27 (1.94-11.48) | 0.90 (0.023-5.03) | 3.12 (1.25-6.42) |
| NNH for the first dose (95% CI) | 18 975 (8711-51 546) | 111 111 (19 881-4 347 826) | 32 051 (15 576-80 000) |
| Cases after second dose, No./recipients of second dose, total No. | 32/82 011 | 4/80 507 | 36/162 518 |
| Incidence after second dose per 100 000 persons (95% CI) | 39.02 (26.69-55.08) | 4.97 (1.35-12.72) | 22.15 (15.51-30.67) |
| NNH for the second dose (95% CI) | 2563 (1816-3747) | 20 121 (7862-74 074) | 4515 (3261-6447) |

Abbreviation: NNH, number needed to harm.

28.63) per 100 000 persons to 0 cases in 22 245 adolescents vaccinated at implementation of the single-dose policy. The 40 167 prepolicy first dose recipients did not receive the second dose because of the single-dose policy. Based on the number needed to harm of the second dose, an estimated 8.90 (95% CI, 6.23-12.32) myocarditis cases were prevented.

Discussion | In this cohort study, the single-dose regimen was found to be associated with reduction in myocarditis risk among vaccinated adolescents. Limitations include sample size during the postpolicy period. Since May 2021, no local transmission of SARS-CoV-2 has occurred in Hong Kong, with stringent nonpharmaceutical interventions. Among the 343 700 adolescents in Hong Kong, no COVID-19-related death has been reported, and the only one admitted to the pediatric intensive care unit due to COVID-19 was an imported case,⁵ indicating that the risk of death or complications from COVID-19 is extremely low among adolescents in Hong Kong. Vaccination policy for adolescents should consider the trade-off between risks and benefits. In countries with large outbreaks and to prevalent local transmission, the risk-benefit assessment would favor a 2-dose regimen because the single-dose regimen provides suboptimal protection from severe outcomes

associated with COVID-19. However, in settings with no evident local transmission and stringent infection control policies, single-dose mRNA vaccination might be a viable option for offering protection to adolescents from severe outcomes associated with COVID-19.

Nevertheless, questions remain about the mechanism of myocarditis following mRNA vaccine. Potential ways to reduce myocarditis risk in adolescents could be the use of single-dose only, a lower dosage for 2 doses as recommended for children aged 5 to 11 years,⁶ or a lengthened interval between doses. More laboratory, trial, and postmarketing data may become available to answer these questions. Our study expands the current understanding of dose-response relationship and suggests that COVID-19 vaccination recommendations in adolescents may need to be customized rather than standardized to fit all.

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COMMENT & RESPONSE

Inhaled Corticosteroids and Long-Acting β_2 Receptor Agonists for Preterm-Born Children—New Insights but Still Many Questions

To the Editor We read with interest the article by Goulden et al¹ on the effect of inhaled corticosteroids (ICS) combined with long-acting β_2 agonists (LABA) in preterm-born children. It is well established that children and adults born preterm have persistently lower than normal lung function, but there is a lack of agreement as to the appropriate respiratory treatment for such individuals. Evidence to support the use of ICS is still lacking.² Goulden et al¹ found that 12 weeks of treatment with fluticasone and salmeterol increased the forced expiratory volume in 1 second (%FEV₁) compared with baseline. However, lung function only improved significantly in patients treated with both ICS and LABA, not in those treated with ICS alone. No LABA-only group was considered to discriminate the anti-inflammatory from the bronchodilator effect, so we cannot know whether the improvement in %FEV₁ was because of the combined effect of ICS and LABA or to LABA alone. The authors¹ provided no information about any respiratory symptoms before and after treatment.

The presence of a chronic airway inflammation is crucial to the debate on the use of ICS, in which many questions remain unanswered, largely because of a lack of airway histological specimens to define the underlying mechanisms as preterm and individuals with bronchopulmonary dysplasia grow older. Data obtained from bronchial biopsies³ and bronchoalveolar lavage⁴ in adolescents and young adults with bronchopulmonary dysplasia show higher proportions of activated CD8⁺ T cells, lower proportions of CD4⁺ T cells, and no eosinophilic inflammation. These findings suggest against type 2 airway inflammation, a known predictor of corticosteroid responsiveness. This is confirmed by an extensive meta-analysis by Course et al quoted in the article by Goulden et al,¹ which found similar FE_{NO} levels in preterm-born and term-born children, pointing to a mechanism other than eosinophilic inflammation being behind wheezing symptoms and airway obstruction in preterm-born individuals.

The authors¹ considered a 10% absolute increase in %FEV₁ a clinically meaningful outcome, but the joint American Thoracic Society and European Respiratory Society recommen-