Comparing self-reported reactogenicity between adolescents and adults following the use of BNT162b2 (Pfizer-BioNTech) messenger RNA Covid-19 vaccine: a prospective cohort study

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HIGHLIGHTS

- Marked age differences in adverse reaction risks from BNT162b2 vaccination
- Moderately increased risks from BNT162b2 in adolescents compared to adults
- Self-reported adverse reactions peaked on first follow-up day after vaccination

Comparing self-reported reactogenicity between adolescents and adults following the use of BNT162b2 (Pfizer-BioNTech) messenger RNA Covid-19 vaccine: a prospective cohort study

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ABSTRACT

Objectives: Although clinical data have shown that the BNT162b2 vaccine, which is widely used in many countries, is safe and effective as a protection against the Covid-19 infection, extant research in adverse reactions using real-world data of various socio-demographic characteristics is scant.

Methods: We conducted a prospective cohort study to compare age differences in self-reported reactogenicity of BNT162b2 in Hong Kong. A total of 1,516 participants were intensively followed up for two weeks following both doses of BNT162b2 vaccination, during which their basic demographic, health conditions, and medication information were collected.

Results: Results from generalized mixed model showed that compared with adults aged 18 – 59, older adults aged 60 or above had a lower risk of adverse reactions, and adolescents aged 12 – 17 had a moderately higher risk.

Conclusions: Results of this study should be informative to parents considering BNT162b2 vaccination for their children in that moderately increased reactogenicity compared with adults is anticipated.

Keywords: Covid-19, vaccine safety, pharmacovigilance, epidemiology, paediatrics

The BNT162b2 messenger RNA Covid-19 vaccine, widely used in more than 100 countries worldwide, has been shown to be safe and effective in protecting populations from the infection of SARS-CoV-2 (Polack et al., 2020; Thomas et al., 2021; Walsh et al., 2020). According to clinical trial data, more than 80% of BNT162b2 recipients reported post-vaccination adverse reactions such as pain and tiredness, although an extremely small proportion of these reactions required medical interventions (Polack et al., 2020). Current research seldom examined such adverse reactions in sub-populations of various socio-demographic characteristics, however.

Since the emergency use of BNT162b2 in adolescents aged 12 or above has been approved in an increasing number of jurisdictions worldwide with few substitutes (Frenck et al., 2021), its self-reported reactogenicity as compared to adult recipients in real-world settings should be examined to better inform parents' decision to permit their children to receive the vaccine (Musa et al., 2021). This study aimed to assess the potential risk differences in the self-reported reactogenicity of BNT162b2 among adolescents, middle-aged adults, and older adults.

METHODS

A prospective cohort design with self-reported data was adopted for this study. Data were collected on the first-dose vaccination day as baseline. Participants were then followed up on the first, second, third, seventh, and the fourteenth day following both doses of vaccination. Basic demographic, health conditions, and medication information were collected during baseline and any self-report adverse reactions were collected throughout the observation period*.

Generalized linear mixed model was performed to examine the association between age group and self-reported adverse reactions[†], adjusting for person-level and measurement-level covariates[‡]. Listwise deletion was applied for missing data due to its relatively negligible proportion. Odds ratios and confidence intervals were obtained for comparisons of risks between

the trichotomized age groups (adolescents 12–17 years; middle-aged adults 18–59 years; and elderly 60 years or above) at .05 significant level by R (version 4.1.1).

RESULTS

As of 12th August 2021, we recruited 2,531 participants (1,016 aged 12-17 years, 759 18-59 years, and 756 60 years or above) who had received BNT162b2. The follow-up success rates of our study were 90.6%, 96.7%, and 72.0% for the adolescent, middle-aged adult, and older adult groups respectively. Details of cohort characteristics are shown in Table 1.

[Insert Table 1 here]

Among all participants, 1,516 (59.90%) reported the experience of adverse reactions after the first dose, and 1,278 (50.49%) reported adverse reactions following the second. The rates of adverse reactions on the seventh follow-up day of first dose were 4.94%, 5.86%, and 5.71% (same day after second dose: 7.12%, 8.29%, and 7.72%) for adolescents, adults, and older adults respectively. For all examined age groups, the proportion of participants reporting any type of adverse reactions peaked on the first follow-up day (first dose: 63.44%; second dose: 62.22%) after both doses of vaccination and gradually declined, with only very few reports of adverse reactions towards the 14th day of follow-up (first dose: 4.44%; second dose: 4.12%).

Results from generalized linear mixed model indicated that compared with middle-aged adults, older adults had reduced odds in any adverse reactions [adjusted odds ratio (aOR) = 0.557, 95% CI 0.440–0.706], local adverse reactions (aOR = 0.469, 95% CI 0.362–0.608), and systemic adverse reactions (aOR = 0.472, 95% CI 0.365–0.611). For the adolescent group, results showed there were increased risks in any (aOR = 1.411, 95% CI 1.096–1.816), local (aOR = 1.343, 95% CI 1.020–1.770), and systemic (aOR = 1.427, 95% CI 1.088–1.874) adverse reactions. Estimates for severe adverse reactions were imprecise due to relatively low incidence for both adolescents and older adults. The model results are summarized in Figure 1.

[Insert Figure 1 here]

DISCUSSIONS

While previous clinical trials have reported the reactogenicity of BNT162b2 (Frenck et al., 2021), there has been little existing research reporting the reactogenicity of BNT162b2 in adolescents in the literature. A plausible explanation of the observed age differences is that, consistent with previous research evidence (Woudenberg et al., 2021), the immune response triggered by a viral infection or vaccines in individuals of a younger age is typically stronger than in those of an older age.

Study limitations that need to be taken into consideration include the design of serial self-report online survey, which entails a risk of omitting the follow-up survey of who had more serious adverse reactions and required medical interventions or were even hospitalized, as evidenced by the imperfect response rates. Self-report bias may also exist in the reactogenicity data, which might partially be induced by the educational gap across the age groups.

The results of this study should be informative to parents considering BNT162b2 vaccination for their children in that moderately increased reactogenicity compared with adults is anticipated, and that severe adverse reactions are rare. Considering the entirety of the existing body of knowledge about the reactogenicity and adverse events following the use of BNT162b2, we believe the benefits of receiving the vaccine still far outweigh the associated risks. Findings should inform the choice of vaccine uptake for parents of eligible adolescents.

Footnote:

*Participants aged 18 or above receiving the first dose of BNT162b2 at government-operated community vaccination centers were recruited since vaccine distribution was commenced on 23rd February 2021. For adolescent participants aged 12 – 17, recruitment commenced upon vaccine distribution on 24th June 2021. The data collection period for all age groups ended on 22 August 2021. We supplemented the active in-person recruitment with flyers including a quick-response (QR) link to the online survey distributed at healthcare facilities. The link to follow-up surveys was sent to participants via instant text messages and surveys were conducted online using Qualtrics, an online data collection platform. Only those participants who were scheduled to complete the 14th-day follow-up survey for the second dose according to the recommended interval between the two doses were included in the analysis. Participants could withdraw from the study anytime.

†Self-reported adverse reactions include local (numbness, soreness, pain, swelling, redness, and itch), systemic (sore throat, tiredness, fever, chills, sweating, cough, headache, muscle pain, joint pain, pain in limbs, abdominal pain, diarrhea, nausea, vomiting, poor appetite, insomnia, feeling unwell, enlarged lymph nodes, rash, and temporary one-sided facial drooping), and severe allergic reactions (hypotension, dizziness, itchy skin rash, swelling of face or tongue, and wheezing/shortness of breath).

‡Person-level covariates include sex, educational attainment, number of chronic medications, and a range of specified chronic conditions, namely autoimmune diseases (ankylosing spondylitis, psoriasis, rheumatoid arthritis, systemic lupus erythematosus), cancer (both remission and under treatment), respiratory diseases (asthma, chronic obstructive pulmonary disease, and others), and other common chronic illnesses, including hypertension, hypercholesterolemia, heart disease,

diabetes, stroke, neurological disorders, mental health disorders, liver problems, and kidney problems. At the measurement level, specific follow-up days (vaccination day, first-, second-, third-, seventh-, and fourteenth-day after vaccination) of both doses were also adjusted for given the anticipated day-dependent reactogenicity.

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COMPETING INTERESTS

FTTL has been supported by the RGC Postdoctoral Fellowship under the Hong Kong Research Grants Council. XL has received research grants from the Food and Health Bureau of the Government of the Hong Kong SAR, research and educational grants from Janssen and Pfizer; internal funding from University of Hong Kong; consultancy fee from Merck Sharp & Dohme, unrelated to this work. CSLC has received grants from the Food and Health Bureau of the Hong Kong Government, Hong Kong Research Grant Council, Hong Kong Innovation and Technology Commission, Pfizer, IQVIA, and Amgen; personal fee from Primevigilance Ltd.; outside the submitted work. EYFW has received research grants from the Food and Health Bureau of the Government of the Hong Kong SAR, and the Hong Kong Research Grants Council, outside the submitted work. ICKW reports research funding outside the submitted work from Amgen, Bristol-Myers Squibb, Pfizer, Janssen, Bayer, GSK, Novartis, the Hong Kong RGC, and the Hong Kong Health and Medical Research Fund, National Institute for Health Research in England, European Commission, National Health and Medical Research Council in Australia,

and also received speaker fees from Janssen and Medice in the previous 3 years. EWYC reports honorarium from Hospital Authority, grants from Research Grants Council (RGC, Hong Kong), grants from Research Fund Secretariat of the Food and Health Bureau, grants from National Natural Science Fund of China, grants from Wellcome Trust, grants from Bayer, grants from Bristol-Myers Squibb, grants from Pfizer, grants from Janssen, grants from Amgen, grants from Takeda, grants from Narcotics Division of the Security Bureau of HKSAR, outside the submitted work.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Our study was approved by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster (UW-21-090) and the Department of Health Ethics Committee (LM 21/2021).

Declaration of interests

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

FTTL has been supported by the RGC Postdoctoral Fellowship under the Hong Kong Research Grants Council. XL has received research grants from the Food and Health Bureau of the Government of the Hong Kong SAR, research and educational grants from Janssen and Pfizer; internal funding from University of Hong Kong; consultancy fee from Merck Sharp & Dohme, unrelated to this work. CSLC has received grants from the Food and Health Bureau of the Hong Kong Government, Hong Kong Research Grant Council, Hong Kong Innovation and Technology Commission, Pfizer, IQVIA, and Amgen; personal fee from Primevigilance Ltd.; outside the submitted work. EYFW has received research grants from the Food and Health Bureau of the Government of the Hong Kong SAR, and the Hong Kong Research Grants Council, outside the submitted work. ICKW reports research funding outside the submitted work from Amgen, Bristol-Myers Squibb, Pfizer, Janssen, Bayer, GSK, Novartis, the Hong Kong RGC, and the Hong Kong Health and Medical Research Fund, National Institute for Health Research in England, European Commission, National Health and Medical Research Council in Australia, and also received speaker fees from Janssen and Medice in the previous 3 years. EWYC reports honorarium from Hospital Authority, grants from Research Grants Council (RGC, Hong Kong), grants from Research Fund Secretariat of the Food and Health Bureau, grants from National Natural Science Fund of China, grants from Wellcome Trust, grants from Bayer, grants from Bristol-Myers Squibb, grants from Pfizer, grants from Janssen, grants from Amgen, grants from Takeda, grants from Narcotics Division of the Security Bureau of HKSAR, outside the submitted work.

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Figure 1. Self-reported adverse reactions over 14-day post-vaccination of both doses for adolescents and elders compared with middle-aged adults among BNT162b2 recipients.

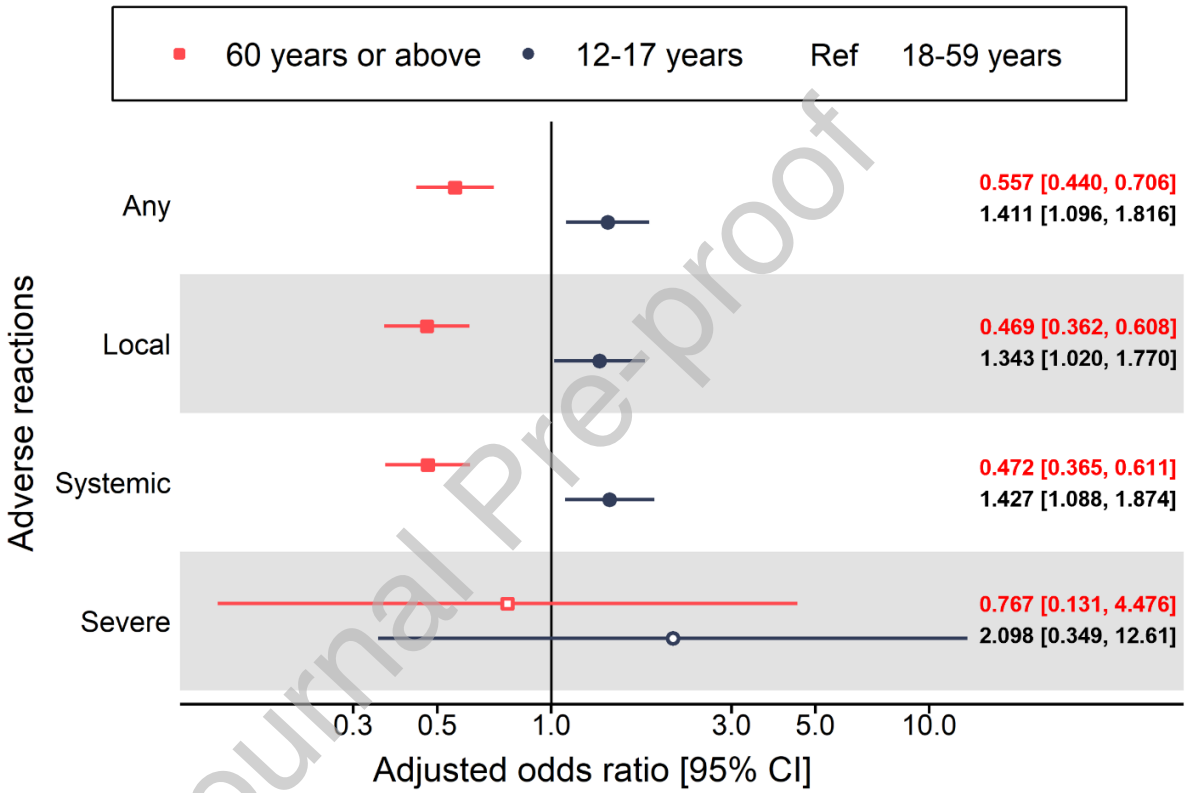

Table 1. Cohort characteristics.

	12 – 17 years	18 – 59 years	60+ years	p-value
n	1016	759	756	
Sex = Male (%)	547 (53.8)	383 (50.9)	397 (52.5)	0.464
Educational attainment (%)				< 0.001
Primary and below	28 (2.8)	4 (0.5)	157 (20.8)	
Secondary	985 (96.9)	139 (18.3)	327 (43.3)	
Post-secondary	1 (0.1)	88 (11.6)	84 (11.1)	
University or above	2 (0.2)	527 (69.5)	188 (24.9)	
Number of chronic medications				< 0.001
None	991 (97.5)	653 (87.0)	297 (39.3)	
1 - 2	23 (2.3)	79 (10.5)	294 (38.9)	
3 - 4	1 (0.1)	15 (2.0)	117 (15.5)	
5 - 9	0 (0.0)	4 (0.5)	45 (6.0)	
10 or more	1 (0.1)	0 (0.0)	3 (0.4)	
Chronic conditions (%)				
Asthma	19 (1.9)	16 (2.1)	10 (1.3)	0.492
Inflammatory bowel disease	0 (0.0)	0 (0.0)	1 (0.1)	0.309
Psoriasis	0 (0.0)	1 (0.1)	3 (0.4)	0.112
Rheumatoid arthritis	1 (0.1)	0 (0.0)	10 (1.3)	< 0.001
Cancer under treatment	1 (0.1)	4 (0.5)	5 (0.7)	0.137
Cancer remission	0 (0.0)	3 (0.4)	15 (2.0)	< 0.001
Hypertension	0 (0.0)	36 (4.7)	294 (38.9)	< 0.001
Hypercholesterolemia	0 (0.0)	19 (2.5)	239 (31.6)	< 0.001
Heart disease	2 (0.2)	5 (0.7)	48 (6.3)	< 0.001
Diabetes	1 (0.1)	15 (2.0)	91 (12.0)	< 0.001
Stroke	0 (0.0)	1 (0.1)	6 (0.8)	0.005
Neurological disorder	0 (0.0)	3 (0.4)	2 (0.3)	0.158
Mental health disorder	5 (0.5)	7 (0.9)	19 (2.5)	< 0.001
Liver problems	0 (0.0)	4 (0.5)	24 (3.2)	< 0.001
Kidney problems	0 (0.0)	3 (0.4)	19 (2.5)	< 0.001
Other chronic conditions	9 (0.9)	31 (4.1)	125 (16.5)	< 0.001