SARS-CoV-2 in Malaysia: A surge of reinfection during the predominately Omicron period

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Throughout the COVID-19 pandemic, SARS-CoV-2 evolved rapidly from the original strain.1 While COVID-19 control measures are relaxed with country’s transition to endemicity, it is imperative to be mindful that as SARS-CoV-2 continues to mutate and circulate, reinfection has also become increasingly common due to the dominance of the highly transmissible variants, immunity evasion, and inadequate preventive strategies from the public because of pandemic fatigue.2 Case surveillance is underpinned by the National Testing Strategy, and comprehensive data of the COVID-19 infection is open access, but the reinfection rate during the Omicron period warrants deeper analysis due to Malaysia’s socio-economic, demographic, and vaccine platform compositions that are more comparable to regional countries. This clarifies the general assumption that COVID-19 infection protects against future infection, despite limited evidence on who is at higher risk and the extent to which booster vaccination protects against reinfection. In this study, we aim to investigate the risk and rate of COVID-19 reinfection across different age group, exposure level, vaccination status and vaccine type. Person-time at risk for reinfection was calculated by subtracting the date of study entry (date of first infection) from date of event (date of reinfection). Individuals with only one infection throughout the study period were censored at the end of study period. Genomic sequencing of COVID-19 sample is highly targeted in countries with known Omicron outbreaks, hence were not representative of variants circulating in the community. To overcome this, a Malaysian study used Bai-Perron sequential breakpoint test on Malaysia’s COVID-19 data to estimate the start of Omicron-dominant period in Malaysia, which was likely in early February 2022.3 Therefore, we determined February 1, 2022 as the breakpoint for the pre-Omicron and Omicron periods. We excluded individuals with single-dose regime and defined individuals to be fully vaccinated with two or three doses at 14 days after the last vaccine date, allowing immunogenicity to develop. We categorized one’s exposure risk based on the frequency that one was tagged as “casual contact” to a SARS-CoV-2 positive case by the Malaysia COVID-19 mobile application contact tracing system (MySejahtera). The automated “casual contact” tracing system in MySejahtera measures exposure because (i) the tagging of contacts is location- and time-specific, with tracing windows calibrated to best predict post-exposure transmission at the location-level and (ii) the positivity rate of “casual contact” is about 10–15% according to surveillance. One becomes a “casual contact” when present in the same premise and time window as another individual who tested positive by the end of the day, hence potentially exposed to SARS-CoV-2. Low exposure is defined if a person was not flagged as “casual contact” throughout the follow-up period; moderate exposure if flagged 1–5 times; and high exposure if flagged more than 5 times. All analysis

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were performed in R version 4.2.1 and Stata version 13 (Statacorp LP).

We included 3,432,651 COVID-19 positive cases that were recorded throughout the study period. Among these, 62,522 (1.8%) had at least one episode of reinfection. There was a drastic increase in reinfection case during the Omicron period relative to pre-Omicron period. (Supplementary Figure 1) In overall, the reinfection incidence rate was 6.6 times higher during the Omicron period compared to the pre-Omicron period (0.69 [95% CI 0.67 – 0.71] vs 4.55 [95% CI 4.51 – 4.58] per 100-person years [PY]) regardless of age group and exposure risk. (Supplementary Table 1) High exposure individuals in the 18–59 age group had a

| Subgroups | Case | Population | PY at risk | Forest plot | Incidence rate per 100 PY (95% CI) | P value* |
|-----------|------|------------|------------|-------------|-----------------------------------|---------|
| Low exposure | | | | | | |
| Age Group <18 | noVax | 5,443 | 632,087 | 292,693 | $\longrightarrow$ | 3.86 (1.81 – 1.91) | 0.019 |
| | oneDose | 89 | 28,465 | 1,393 | $\longrightarrow$ | 2.03 (1.65 – 2.49) | 0.033 |
| | twoDose | 106 | 51,750 | 7,125 | $\longrightarrow$ | 1.49 (1.23 – 1.80) | ref |
| Age Group 18-59 | noVax | 3,263 | 246,181 | 150,057 | $\longrightarrow$ | 2.17 (2.10 – 2.25) | 0.001 |
| | oneDose | 979 | 59,078 | 35,211 | $\longrightarrow$ | 2.78 (2.61 – 2.96) | 0.019 |
| | twoDose | 2,199 | 243,059 | 84,079 | $\longrightarrow$ | 2.62 (2.51 – 2.73) | 0.027 |
| | threeDose | 216 | 84,852 | 7,019 | $\longrightarrow$ | 3.38 (2.69 – 3.52) | ref |
| Age Group ≥ 60 | noVax | 590 | 57,102 | 35,738 | $\longrightarrow$ | 1.65 (1.52 – 1.79) | 0.015 |
| | oneDose | 264 | 17,320 | 11,112 | $\longrightarrow$ | 2.38 (2.12 – 2.68) | 0.004 |
| | twoDose | 842 | 112,196 | 48,831 | $\longrightarrow$ | 1.88 (1.76 – 2.01) | 0.027 |
| | threeDose | 75 | 43,551 | 3,897 | $\longrightarrow$ | 1.92 (1.53 – 2.41) | ref |
| Moderate exposure | | | | | | |
| Age Group <18 | noVax | 776 | 33,006 | 21,305 | $\longrightarrow$ | 3.45 (3.21 – 3.71) | 0.001 |
| | oneDose | 60 | 2,808 | 1,150 | $\longrightarrow$ | 5.22 (4.05 – 6.72) | 0.001 |
| | twoDose | 82 | 22,338 | 3,038 | $\longrightarrow$ | 3.7 (2.17 – 3.35) | ref |
| Age Group 18-59 | noVax | 10,754 | 261,951 | 191,035 | $\longrightarrow$ | 5.63 (5.52 – 5.74) | 0.001 |
| | oneDose | 5,039 | 130,617 | 81,112 | $\longrightarrow$ | 6.21 (6.04 – 6.39) | 0.001 |
| | twoDose | 10,293 | 554,032 | 190,667 | $\longrightarrow$ | 5.4 (5.29 – 5.50) | 0.001 |
| | threeDose | 1,439 | 341,405 | 29,660 | $\longrightarrow$ | 4.85 (4.61 – 5.11) | ref |
| Age Group ≥ 60 | noVax | 269 | 11,031 | 8,763 | $\longrightarrow$ | 3.07 (2.72 – 3.46) | 0.007 |
| | oneDose | 142 | 6,451 | 4,359 | $\longrightarrow$ | 3.26 (2.76 – 3.84) | 0.004 |
| | twoDose | 440 | 39,001 | 16,698 | $\longrightarrow$ | 2.64 (2.42 – 2.85) | 0.029 |
| | threeDose | 63 | 32,663 | 2,958 | $\longrightarrow$ | 2.73 (2.30 – 2.73) | ref |
| High exposure | | | | | | |
| Age Group <18 | noVax | 70 | 999 | 664 | $\longrightarrow$ | 10.55 (8.35 – 13.33) | 0.015 |
| | oneDose | 1 | 63 | 27 | $\longrightarrow$ | 3.77 (0.51 – 20.75) | 0.736 |
| | twoDose | 7 | 944 | 121 | $\longrightarrow$ | 5.77 (2.75 – 12.10) | ref |
| Age Group 18-59 | noVax | 7,066 | 72,721 | 54,183 | $\longrightarrow$ | 13.04 (12.74 – 13.35) | 0.001 |
| | oneDose | 3,784 | 38,687 | 24,345 | $\longrightarrow$ | 15.34 (15.06 – 15.62) | 0.001 |
| | twoDose | 6,871 | 153,042 | 49,948 | $\longrightarrow$ | 13.76 (13.41 – 14.10) | 0.001 |
| | threeDose | 1,117 | 144,989 | 13,600 | $\longrightarrow$ | 8.21 (7.75 – 8.71) | ref |
| Age Group ≥ 60 | noVax | 59 | 1,368 | 1,122 | $\longrightarrow$ | 5.26 (4.08 – 6.79) | 0.046 |
| | oneDose | 40 | 743 | 307 | $\longrightarrow$ | 7.88 (5.78 – 10.25) | 0.001 |
| | twoDose | 110 | 3,962 | 1,659 | $\longrightarrow$ | 6.63 (5.20 – 7.99) | 0.002 |
| | threeDose | 15 | 5,216 | 499 | $\longrightarrow$ | 3.01 (1.84 – 4.99) | ref |

*P value is calculated based on the incidence rate ratio of the unvaccinated, one dose or two doses against the reference group booster dose in each subgroup.

For age group <18 subgroups, the reference group is those who had fully vaccinated with two doses.

Table 1: Reinfection incidence rate up to Omicron period, stratified by age group, exposure risk and vaccination status.

PY, Person-years; noVax, not vaccinated; oneDose, received 1 dose of vaccine; twoDose, received 2 doses of vaccine; threeDose, received third dose of vaccine as booster dose. Low exposure means the individual was not flagged as “casual contact” throughout follow up period; moderate exposure means the individual was flagged 1–5 times; high exposure means the individual was flagged more than 5 times.

2 www.thelancet.com Vol 26 September, 2022
remarkably higher incidence rate and the rates were significantly different in two periods (13.26 [95% CI 13.07–13.45] during Omicron vs 13.4 [95% CI 1.27–1.42] during pre-Omicron per 100-PY). (Supplementary Table 1).

Booster vaccination was highly advocated in Malaysia’s national vaccination campaign and is eligible from October 2021 onwards for those aged 18 years and above. The different regimes of vaccine combinations are shown in Supplement Figure 2. Briefly, Pfizer-BioNTech mRNA vaccine and AstraZeneca viral vector vaccine were the main recommendations by Ministry of Health for booster vaccination, whereas Sinovac inactivated virus vaccine were only offered for homologous boosting or to those who cannot tolerate the former. We found that the third dose vaccination reduced the reinfection rate for all adults with moderate and high exposure risk (Table 1). The reinfection rate was significantly lower among the high exposure, 18–59 years old, boosted adults than the unvaccinated and two-dose group (8.21 [95% CI 7.75 – 8.71] vs 13.04 [95% CI 12.75–13.35]) and 13.76 [95% CI 13.43 – 14.09] per 100 PY) (Table 1). Among those who received booster dose, homologous regimes and heterologous regime with Pfizer vaccine have significantly lower reinfection rates than heterologous regimes with AstraZeneca (Table 2). For individuals with low exposure risk, the reinfection rate was not significantly different by vaccination status (Table 1).

We have three main messages. First, reinfection has become more common in Malaysia during the Omicron period. This trend is consistent with other countries, some with evidence of multiple reinfections. The mutated and highly transmissible strain circulating in the community leads to higher infection rate and hence higher chance for reinfection to occur. Second, reinfection rates were higher among adults 18–59 years of age and those with high exposure. People naturally have increased exposure when they regain pre-pandemic mobility and start frequenting public places as the society reopened. It is important to raise this awareness and maintain persistent efforts to remind the public to remain vigilant because the risk of reinfection still lurks if cautionary steps are not followed. Up to the point of analysis, homologous regimes and heterologous booster with Pfizer conferred better protection against reinfection for this risk group and should be encouraged. Lastly, booster vaccine, however, does not further reduce the reinfection rate in low exposure group. This poses the questions whether a second booster will be of additional benefit to those with low exposure. There may be residual confounding factors that are masking the benefit of vaccination among this group, such as underlying comorbidities (people with comorbidities and the elderly tend to stay home to avoid exposure) and more relaxed preventive measures among household members. Members living in the same household as COVID-19 case are susceptible to infection, even if not tagged as “casual contact” by MySejahtera, because of close proximity and caring duties for infected member.

In conclusion, the surge in reinfection rate was consistent with the emergence of the Omicron variant and the reinfection risk was higher among high exposure, 18–59 years old and unboosted group. As more economic sectors reopen, the SAR-CoV-2 viruses are expected to continue mutating and circulating. The existing COVID-19 surveillance system may need to be appropriately adapted to detect the epidemiological signals of (re)infection cases and immunity evasion by newer variants for any alarming surge. Apart from booster vaccination, public health messaging should convey the reinfection risk to the general public and advocate for risk mitigation measures supported by the social and behavioural sciences.

Contributors
All authors had full access to all the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis. Conceptualization and design: SLY, HST, WYH. Data acquisition: JLS, MH. Data cleaning and analysis: SLY, HST, WYH. Data interpretation: All authors. Drafting of manuscript:
HST, SLY. Critical revision and approval of the manuscript for important intellectual content: All authors. Supervision: WYH.

Data sharing statement
The dataset analysed for the current study are available from corresponding author upon reasonable request.

Declaration of interests
All authors declare no conflict of interest.

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Ethics Approval
The study was approved by the Medical Research and Ethics Committee (MREC) Ministry of Health Malaysia and registered (NMRR-21-1660-60697).

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