**Supplementary Material**

We conducted sensitivity analyses to estimate the time-dependent proportion of the population that is immune to symptomatic SARS-CoV-2 infection by applying three different scenarios: 1) the immunity elicited by natural infection wanes at the same rate as that elicited by the second vaccine dose; 2) the immunity elicited by natural infection wanes at a rate that depends on the dominant SARS-CoV-2 variant in circulation; and 3) there was no emergence of the Omicron variant or booster vaccine rollout.

**Sensitivity analysis 1.**

We assumed that the infection-induced immunity against symptomatic infection with the Omicron variant wanes in a fashion identical to that of the immunity induced by the second vaccine dose. The results of this analysis are shown in Figure S1 and Table S1.

Chart

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**Figure S1.** **Age-specific proportion of the population that is immune to symptomatic SARS-CoV-2 infection, February 17, 2021–August 1, 2022.**

(A–F) The lines show the time-dependent proportion of the population that is immune to symptomatic infection among people aged from 20–29 (A), 30–39 (B), 40–49 (C), 50–59 (D), 60–69 (E), and ≥70 (F) years, and the shaded areas are their 95% confidence intervals (CIs), computed via the bootstrapping method. The red lines reflect the scenarios in which the immunity from natural infection as well as the immunity from the second and third vaccine doses are considered, whereas the light blue lines reflect the scenarios in which only the immunity from the second and third vaccine doses is taken into account.

**Table S1. Age-specific proportion of the population immune to symptomatic SARS-CoV-2 infection on April 10, June 1, and August 1, 2022.**

The values represent the proportion of the population that is immune to symptomatic infection with the Omicron variant, when considering both immunity derived from vaccination and that induced by natural infection. The numbers in parentheses show the 95% confidence intervals as computed by the parametric bootstrap method.

|  |  |  |  |
| --- | --- | --- | --- |
| Age group | 2022/4/10 | 2022/6/1 | 2022/8/1 |
| 20–29 | 35 (34.6–35.4) | 40.9 (40.5–41.3) | 37.2 (36.6–37.9) |
| 30–39 | 33.2 (32.8–33.6) | 39.8 (39.4–40.2) | 36.4 (35.7–37.0) |
| 40–49 | 35.5 (35.1–35.9) | 43.8 (43.3–44.2) | 36.2 (35.4–36.9 |
| 50–59 | 42.3 (41.9–42.8) | 39.6 (39.0–40.1) | 28.0 (27.2–28.8) |
| 60–69 | 48.5 (48.0–49.0) | 36.8 (36.1–37.4) | 25.8 (24.8–26.7) |
| ≥70 | 51.3 (50.8–51.8) | 38.0 (37.2–38.9) | 27.0 (25.9–28.0) |

**Sensitivity analysis 2.**

Within the study period, the dominant variant of SARS-CoV-2 in Japan changed from Delta to Omicron; this change took place from December 2021 to January 2022. We assumed that SARS-CoV-2 cases that occurred up through December 31, 2021 were caused by infection with Delta and those that occurred from January 1, 2022 onward were caused by infection with Omicron (Ministry of Health Labour and Welfare, 2021). We then assumed that the decay rates of immunity gained by infection with the Delta or Omicron variants are identical to those of immunity induced by the second and third vaccine doses, respectively. It should be noted that the immunity shown here represents protection against symptomatic infection with Omicron, which was the dominant variant when this analysis was conducted. The results of this analysis are presented in Figure S2 and Table S2.

Chart

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**Figure S2.** **Age-specific proportion of the population that is immune to symptomatic SARS-CoV-2 infection, February 17, 2021–August 1, 2022.**

(A–F) The lines show the time-dependent proportion of the population that is immune to symptomatic infection among people aged from 20–29 (A), 30–39 (B), 40–49 (C), 50–59 (D), 60–69 (E), and ≥70 (F) years, and the shaded areas are their 95% confidence intervals (CIs), computed via the bootstrapping method. The red lines reflect the scenarios in which the immunity from natural infection as well as the immunity from the second and third vaccine doses are considered, whereas the light blue lines reflect the scenarios in which only the immunity from the second and third vaccine doses is taken into account.

**Table S2. Age-specific proportion of the population immune to symptomatic SARS-CoV-2 infection on April 10, June 1, and August 1, 2022.**

The values represent the proportion of the population that is immune to symptomatic infection with the Omicron variant, when considering both immunity derived from vaccination and that induced by natural infection. The numbers in parentheses show the 95% confidence intervals (CIs) as computed by the parametric bootstrap method.

|  |  |  |  |
| --- | --- | --- | --- |
| Age group | 2022/4/10 | 2022/6/1 | 2022/8/1 |
| 20–29 | 41.8 (41.4–42.2) | 50.2 (49.8–50.6) | 46.1 (45.5–46.8) |
| 30–39 | 38.7 (38.4–39.2) | 47.6 (47.2–48.0) | 43.9 (43.2–44.5) |
| 40–49 | 39.7 (39.3–40.1) | 49.8 (49.3–50.2) | 36.2 (35.4–36.9) |
| 50–59 | 45.2 (44.8–45.6) | 43.5 (43.0–44.1) | 41.9 (41.1–42.7) |
| 60–69 | 50.2 (49.7–50.7) | 39.1 (38.4–39.8) | 31.8 (31.0–32.6) |
| ≥70 | 52.8 (52.2–53.2) | 39.9 (39.1–40.8) | 28.8 (27.7–29.8) |

**Sensitivity analysis 3.**

We estimated the maximum and waning rate of protection conferred by the BNT162b2 vaccine against symptomatic infection with the Delta variant, using the same methods described in the manuscript. For this analysis, we used the same data on time-dependent vaccine effectiveness obtained from a published study (Andrews et al., 2022) that was used in the main text. The parameters in the immune decay function (i.e., the maximum vaccine effectiveness) and (i.e., the waning speed of vaccine effectiveness) were estimated to be 0.95 (95% CI: 0.94–0.96) and 0.0022 (95% CI: 0.0022–0.0024), respectively (Figure S3). Assuming the immunity from the second vaccine dose and that from natural infection both wane following this estimated decay function (note: as stated in the main manuscript, the maximum effectiveness for natural infection was fixed as 1 (i.e., )), we estimated the proportion of the population that is immune to symptomatic infection with the Delta variant from February 17, 2021 to February 31, 2022 (Figure S4).

Chart, line chart

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**Figure S3. Estimated time-dependent waning of immunity against symptomatic infection with the Delta variant after the second vaccine dose.**

The blue line shows the estimated vaccination effectiveness, with the shaded area representing the 95% confidence interval (CI) derived by bootstrapping. The points represent the vaccine effectiveness against symptomatic infection, with the error bars displaying their 95% CIs, according to data from a published study (Andrews et al., 2022).

Chart, line chart

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**Figure S4.** **Age-specific proportion of the population that is immune to symptomatic infection with the Delta variant, February 17, 2021–August 1, 2022.**

(A–F) The lines show the time-dependent proportion of the population that is immune to symptomatic infection with the Delta variant among people aged from 20–29 (A), 30–39 (B), 40–49 (C), 50–59 (D), 60–69 (E), and ≥70 (F) years, and the shaded areas are their 95% confidence intervals (CIs), computed via the bootstrapping method. The red lines reflect the scenarios in which the immunity from natural infection as well as the immunity from the second and third vaccine doses are considered, whereas the light blue lines reflect the scenarios in which only the immunity from the second and third vaccine doses is taken into account.

**Table S3. Age-specific proportion of individuals immune to symptomatic SARS-CoV-2 infection at the end of February 2022.**

The values in V and V + I represent the proportion of people immune to symptomatic infection with the Delta variant when considering immunity from solely the second vaccine dose and when considering immunity from both vaccination and natural infection, respectively. The numbers in parentheses show the 95% confidence intervals as computed by the parametric bootstrap method.

|  |  |  |
| --- | --- | --- |
|  | 2022/2/28 | |
| Age group | V (95% CI) | V + I (95% CI) |
| 20–29 | 53.8 (53.3–54.2) | 76.2 (75.7–76.6) |
| 30–39 | 51.8 (51.3–52.2) | 68.4 (67.9–68.8) |
| 40–49 | 52.4 (51.9–52.8) | 64.9 (64.4–65.4) |
| 50–59 | 56.6 (56.0–57.1) | 65.6 (65.0–66.1) |
| 60–69 | 55.4 (54.7–56.0) | 60.6 (60.0–61.3) |
| ≥70 | 52.9 (52.0–53.7) | 57.2 (56.3–58.0) |

**References**

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