Clinical Infectious Diseases

MAJOR ARTICLE

Vaccine Coverage Associated With Ending a Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Wave: A Retrospective Longitudinal Analysis

Aharona Glatman-Freedman,[1,2] Sarah F. Feldman,[3] Yael Hershkovitz,[1] Zalman Kaufman,[1] Rita Dichtiar,[1] Lital Keinan-Boker,[1,4] and Michal Bromberg[1,2]

[1]Israel Center for Disease Control, Ministry of Health, Ramat Gan, Israel; [2]Department of Epidemiology and Preventive Medicine, School of Public Health, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; [3]National Institute for Antibiotic Resistance and Infection Control, Ministry of Health, Tel Aviv, Israel; and [4]School of Public Health, Haifa University, Haifa, Israel

Background. Two SARS-CoV-2 waves in Israel ended while a substantial number of individuals remained unvaccinated or partially vaccinated. The indirect protective effect of the first BNT162b2 vaccination campaign in Israel was evaluated between 22 December 2020 and 18 May 2021.

Methods. The daily percentage of new polymerase chain reaction (PCR)–confirmed SARS-CoV-2 cases among unvaccinated individuals was analyzed for trends. Major shifts were identified using piecewise linear regression analysis. At these shifts, the percentage of naturally vaccinated (past SARS-CoV-2 cases) and the percentage of actively vaccinated (by inoculation) individuals were weighted and summed to determine the percentage of natural and active vaccination (NAV).

Results. A first decline among unvaccinated individuals occurred during a lockdown period, when the percentage of NAV was 8.16%. The major decline occurred after the end of the lockdown when the percentage of NAV reached 52.05%. SARS-CoV-2 cases ultimately declined among unvaccinated individuals when the percentage of NAV reached 63.55%. During the study period, the Alpha variant was prevalent and the use of nonpharmaceutical interventions, including social distancing, existed to varying degrees.

Conclusions. The vaccination campaign played a major role in the decline of SARS-CoV-2 infection among unvaccinated individuals, leading to the end of the first 2021 SARS-CoV-2 wave (Alpha variant) in Israel. Infection in unvaccinated individuals stopped when two-thirds of the population were naturally or actively vaccinated. Any change in characteristics of the virus or the population can lead to a new outbreak.

Keywords. indirect protection; SARS-CoV-2; vaccination.

Large vaccination campaigns against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been carried out around the world since the end of 2020. However, despite considerable efforts, pandemic control has not been achieved. By 1 December 2021, Israel underwent 2 SARS-CoV-2 waves since national vaccination efforts began. The end of these first and second waves was associated with an increase in the second-dose vaccine coverage and with an increase in the booster-dose coverage, respectively. However, both waves subsided while a substantial number of individuals remained unvaccinated or partially vaccinated.

While direct protection consists of the reduction in infection among individuals who are vaccinated or naturally infected, indirect vaccine protection consists of the reduction in infection in unvaccinated individuals of the same population [1]. When a substantial share of the population becomes immune to an infectious disease through recovery from infection or through vaccination, and individuals who are not immune become indirectly protected, herd immunity occurs [2]. Indirect vaccine protection exists when the vaccine protective effect in a population exceeds the expected protection, which depends on the level of vaccine coverage and protective efficacy [1].

The population vaccine coverage required to attain indirect protection varies by disease. While indirect protection for measles is attained once approximately 95% of the population aged 5 years and younger is vaccinated [3, 4], approximately 80% is required for mumps [5].

Israel's SARS-CoV-2 vaccine campaign started on 20 December 2020 and relied on the BNT162b2 vaccine (Pfizer-BioNTech), which was shown to have high vaccine efficacy and vaccine effectiveness (VE) in 2-dose recipients [6–10]. A substantial reduction in the SARS-CoV-2 wave, predominated by the B.1.1.7 (Alpha) variant [11], was observed following vaccine introduction. On 18 May 2021, only 19 new SARS-CoV-2 laboratory-confirmed cases were detected in Israel (2 cases per 1 million population), 4 SARS-CoV-2–positive patients were hospitalized, and no deaths occurred. Thus, population-level

Received 02 February 2022; editorial decision 20 June 2022; published online 10 August 2022

Correspondence: A. Glatman-Freedman, The Israel Center for Disease Control, Gertner Institute Building, Tel Hashomer, Ramat Gan, 5265601, Israel (aharona.freedman@ moh.gov.il).

Clinical Infectious Diseases® 2023;76(3):e207–e15

https://doi.org/10.1093/cid/ciac524

protection from SARS-CoV-2 in Israel was apparently achieved. The protective effect was short as a new SARS-CoV-2 wave, predominated by the B.1.617.2 (Delta) variant [11], started in the third week of June 2021, associated with waning of vaccine-induced protection [12, 13].

We sought to characterize the indirect effect of the BNT162b2 vaccine during the first SARS-CoV-2 wave (Alpha variant) that occurred while vaccines were available in Israel. Such characterization is important for understanding what percentage of the population needs to be "freshly" vaccinated to end a SARS-CoV-2 wave.

METHODS

Study Design and Data Collection

We performed a retrospective population-based analysis using 2 national data repositories. The national SARS-CoV-2 polymerase chain reaction (PCR) test repository includes the following information for each individual: swab date, results date, and test result. The national SARS-CoV-2 vaccine repository includes the following information for each vaccinated individual: vaccine name, lot number, and administration date. Both repositories also include personal identifiers and demographic data.

The unique personal identity number (UPIN) of each Israeli resident was used to match the repositories. UPINs were twice encrypted. The number of Israeli residents (all ages, n = 9 053 200, and by age group) was based on the 2020 Central Bureau of Statistics statistical abstract [14].

Vaccination and SARS-CoV-2 Status

The daily numbers of individuals vaccinated with 1 or 2 doses and individuals who were SARS-CoV-2–positive by PCR between 22 December 2020 and 18 May 2021 for the entire Israeli population and for the age groups 0–11, 12–15, 16–18, 19–34, 35–49, 50–59, 60–79, and ≥80 years old were retrieved from the repositories.

Individuals who received their first vaccine dose were considered to be 1-dose recipients. Once they received a second dose, they were no longer considered 1-dose recipients, but second-dose recipients only.

Individuals were considered to be SARS-CoV-2–positive from the date of their first positive laboratory PCR result for SARS-CoV-2. A SARS-CoV-2–positive individual who previously received 1 or 2 vaccine doses was considered to be SARS-CoV-2–positive from the date of the positive PCR test result and no longer considered to be a 1- or 2-dose recipient from this date. For individuals having more than 1 SARS-CoV-2–positive PCR test, only the first one was considered in the analysis. The number of unvaccinated individuals for each study date was calculated by omitting the number of Israeli residents who received the relevant (first or second) BNT162b2 vaccine dose from the total number of Israeli residents who did not have a documented SARS-CoV-2–positive test by that date.

Assessment of Vaccination Coverage

To assess the level of partial or full protection against SARS-CoV-2 in Israeli residents, we calculated the cumulative percentage of individuals who had received 1 BNT162b2 vaccine dose, 2 BNT162b2 vaccine doses, or who had a positive PCR test by the date of evaluation.

Dynamics of New SARS-CoV-2 Cases

Daily percentages and the 7-day moving average of percentages of new SARS-CoV-2 cases among individuals who received 1 vaccine dose or 2 vaccine doses or among unvaccinated individuals were calculated. Significant changes in the daily percentage of new SARS-CoV-2 cases among unvaccinated individuals were detected using piecewise linear regression models [15]. The date when a significant change occurred was called a "breakpoint." The "first breakpoint" was the breakpoint preceding the first significant change in slope. The "major decline breakpoint" was the breakpoint preceding the steepest negative slope. The "end of decline" was the last date before a negative value for the percentage of daily SARS-CoV-2 cases was fitted.

Determination of Indirect Protection

To determine the percentage of likely protected individuals due to natural and active vaccination (NAV) resulting from SARS-CoV-2 infection or vaccination, respectively, on a particular breakpoint date, we used the following parameters:

1. Percentage of individuals who had received 2 doses of the BNT162b2 vaccine at least 7 days prior to the particular breakpoint date. This percentage was based on studies that demonstrated a vaccine efficacy of 95% 7 days after receipt of the second dose [6].
2. Percentage of individuals who had received 1 dose of the BNT162b2 vaccine at least 14 days prior to the particular breakpoint date. This percentage was based on studies that demonstrated VE of approximately 50% 14–20 days after receipt of the first dose [9].
3. Percentage of individuals who had a positive SARS-CoV-2 PCR test at least 14 days prior to the particular breakpoint date. This percentage was based on the detection of robust neutralizing antibodies 14 days after the onset of symptoms [16].

Based on these parameters we designed a formula to determine the percentage of likely protected individuals due to NAV, on a particular date:

$$\%NAV(t) = \%VAC2(t-7) + \%VAC1(t-14)/2 + \%SARS\text{-}CoV\text{-}2\text{-}pos(t-14)$$

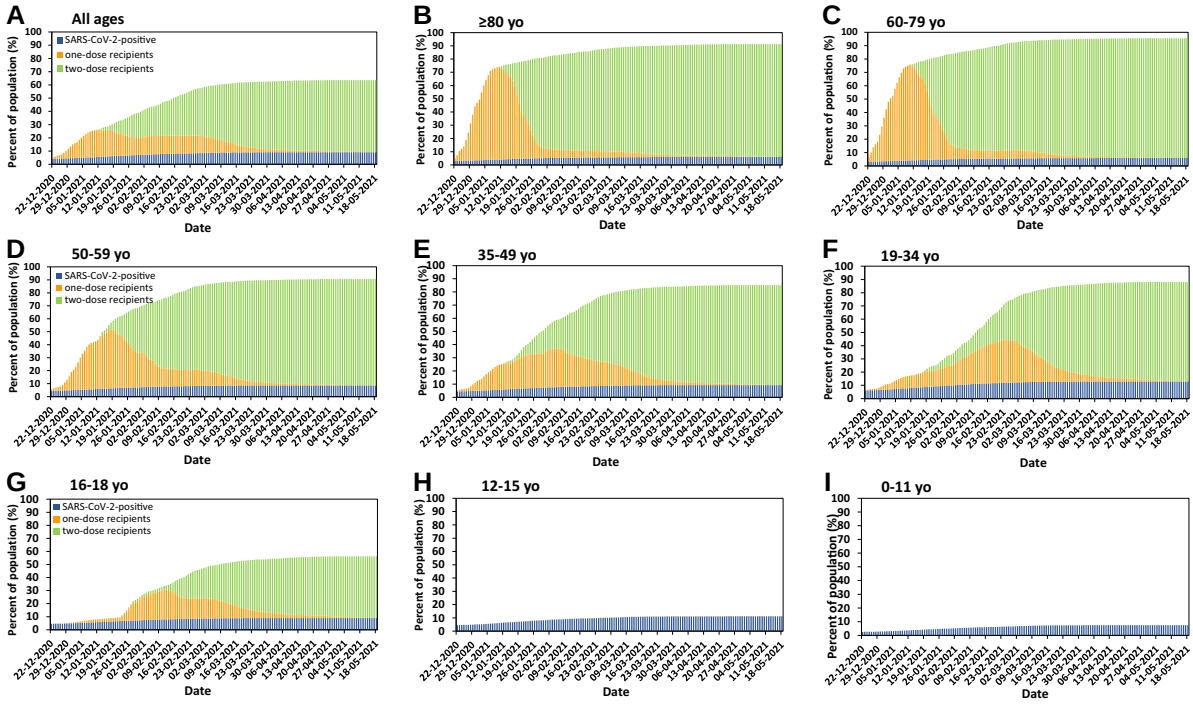

Figure 1. Progression of the percentage of vaccination coverage (actively vaccinated population) and the percentage of SARS-CoV-2–positive cases (naturally vaccinated population) for all ages (*A*) and by age group (*B*–*I*). The panels show the cumulative 2-dose vaccination coverage and the cumulative percentage of SARS-CoV-2–positive individuals. The 1-dose vaccination coverage shown is cumulative until 1-dose recipients receive their second vaccine dose or became SARS-CoV-2–positive, at which point they are no longer counted as 1-dose vaccine recipients. The non-colored area above the bars represents the daily percentage of Israeli residents who were neither vaccinated nor were documented by that date to be SARS-COV-2–infected. Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; yo, years old.

Where t represents the day of NAV determination, *%VAC2(t-7)* is the percentage of second-dose recipients 7 days prior to day t, *%VAC1(t-14)* is the percentage of first-dose recipients 14 days prior to day t, *%SARS-CoV-2-pos(t-14)* is the percentage of SARS-CoV-2 PCR–positive individuals 14 days prior to day t.

%VAC1(t-14) is divided by 2 to represent the fact-based assumption that a single BNT162b2 vaccine dose leads to approximately half of the 2-dose VE (50%) against SARS-CoV-2 infection 14 days after administration [9].

Statistical Analysis

SARS-CoV-2–positive individuals, 1-dose recipients, and 2-dose recipients were expressed as a daily cumulative percentage of the total population. The 7-day moving average of the daily percentage of SARS-CoV-2–positive cases was calculated among unvaccinated and 1-dose and 2-dose recipients. The 7-day moving average of the percentage of hospitalization and death among SARS-CoV-2–positive individuals was calculated for unvaccinated individuals and 2-dose recipients.

Significant changes in the daily percentage of confirmed SARS-CoV-2 cases among unvaccinated individuals throughout the study period were detected using piecewise linear regression analysis [15] applied to the daily percentage (without smoothing) of new PCR-confirmed SARS-CoV-2–positive cases among unvaccinated individuals, using the R package segmented and R version 3.6.1 (R Foundation for Statistical Computing). The number and positions of breakpoints were selected based on the Bayesian information criterion with a maximum of 5 breakpoints. The percentage of NAV was computed as described above for each breakpoint and for the "end of decline." The analyses were carried out for all Israeli residents and by age group.

Ethical Consideration

The use of individual data from the 2 national data repositories was approved by the Superior Ethical Committee of the Israel Ministry of Health (MOH).

RESULTS

Progression of Vaccination Status

Figure 1 demonstrates the evolution of the percentage of vaccination coverage and percentage of SARS-CoV-2–positive individuals throughout the study period for the entire population and by age group. Specifically, it shows the cumulative 2-dose vaccination coverage and the cumulative percentage of

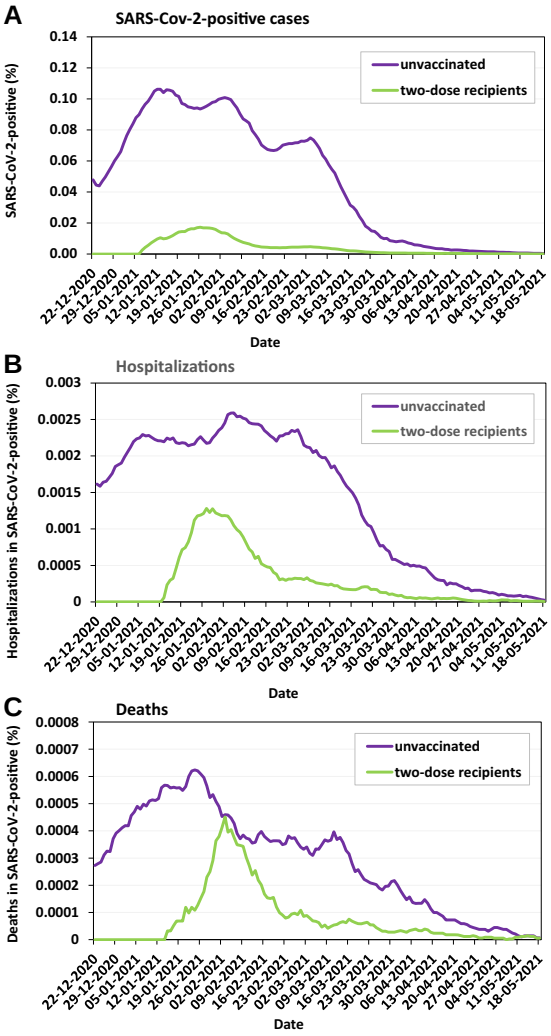

Figure 2. Seven-day moving average of the percentage of new PCR-confirmed SARS-CoV-2–positive cases (*A*), hospitalizations (*B*), and deaths (*C*) of individuals of all ages among 2-dose vaccine recipients and unvaccinated individuals. Abbreviations: PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

SARS-CoV-2–positive individuals that increases over time. The 1-dose vaccination coverage is cumulative until 1-dose recipients receive their second vaccine dose or became SARS-CoV-2–positive, at which point they are no longer counted as 1-dose vaccine recipients.

By 18 May 2021, of the study population, only 35 individuals remained with only 1 vaccine dose (0.004%), and 36.4% were not vaccinated nor had a past SARS-CoV-2 infection (Figure 1*A*).

Dynamics of SARS-CoV-2 Cases

Figure 2 demonstrates the 7-day moving average of the percentage of new SARS-CoV-2–positive cases (Figure 2*A*) and the 7-day moving average of the percentage of hospitalizations (Figure 2*B*) and deaths (Figure 2*C*) among SARS-CoV-2–positive individuals, by vaccination status. The percentages of cases, hospitalizations, and deaths were higher among unvaccinated individuals compared with 2-dose vaccine recipients. The percentage of cases, hospitalizations, and deaths reached a nadir by the end of the evaluation period, both among unvaccinated and 2-dose vaccine recipients. Supplementary Figure 1 shows the daily numbers of SARS-CoV-2 cases as well as hospitalizations and deaths among SARS-CoV-2–positive individuals of all ages, by vaccination status.

Figure 3 demonstrates the 7-day moving average of the percentage of new SARS-CoV-2–positive individuals by vaccination status, for all ages (Figure 3*A*) and by age group (Figure 3*B*–3*I*). The lowest SARS-CoV-2–positive percentage was observed among individuals who received 2 vaccine doses (Figure 3*A*–3*G*). The percentages among unvaccinated individuals aged 19 years and older were higher compared with 1-dose and 2-dose vaccine recipients (Figure 3*A*–3*F*).

Figure 4 shows the results of the piecewise regression analysis. Three breakpoints were identified in the all-ages analysis (Figure 4*A*), and 2 to 3 breakpoints were identified in the age group analyses. An end of decline was observed in all age groups prior to 18 May 2021, except for the 12–15-year-old group.

In all analyses, a substantial increase in the percentage of daily SARS-CoV-2 cases prior to the "first breakpoint" was apparent. After the first breakpoint, the percentage of daily cases either reached a plateau, decreased, or demonstrated a mild increase. All analyses demonstrated a "major decline breakpoint" after which a steep decline was observed. This steep decline was followed by another breakpoint that led to the "end of decline" (Figure 4).

For all ages and for each age group the first breakpoint was different from the major decline breakpoint, with the exception of the 12–15-year and the 16–18-year age groups, where the first breakpoint was also the major decline breakpoint.

For all age groups, the first breakpoint occurred between 7 January and 13 January 2021. For all age groups, with the exception of the 16–18-year and the 12–15-year age groups, the major decline breakpoint occurred between 3 March and 11 March 2021. For all age groups, with the exception of the 12–15-year age group, the end of decline occurred between 7 May and 13 May 2021. For specific dates, see Table 1.

Determination of Indirect Protection

Table 1 demonstrates the percentage of NAV in individuals of all ages and by age groups at the following points of interest: "first breakpoint," "major decline breakpoint," and "end of decline." Specifically, it shows that in all ages the first breakpoint occurred when the percentage of NAV was 8.16%, the major decline breakpoint occurred when the percentage of NAV was 52.05%, and the end of decline occurred when the

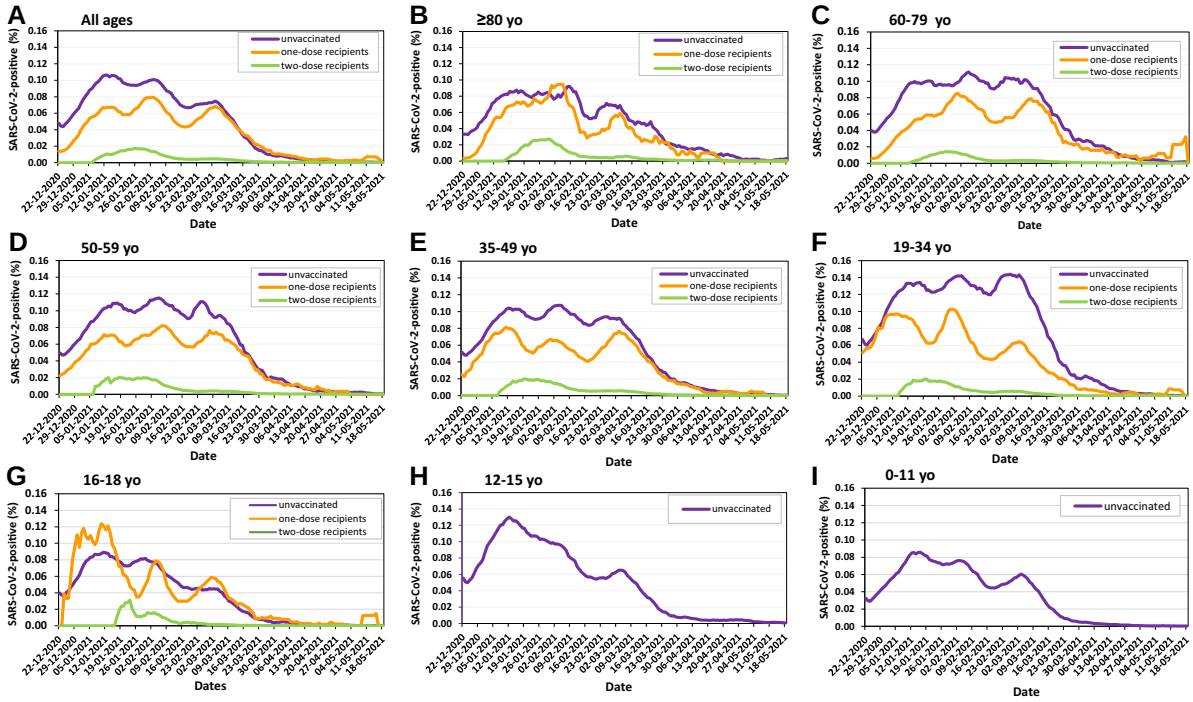

Figure 3. Seven-day moving average of the percentage of new PCR-confirmed SARS-CoV-2–positive cases in individuals of all ages (*A*) and individuals belonging to specific age groups (*B–I*) by vaccination status. Abbreviations: PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; yo, years old.

percentage of NAV reached 63.55%. Supplementary Figure 2 shows the daily NAV superimposed on the data presented in Figure 3.

Use of Nonpharmaceutical Interventions During the Study Period

Various nonpharmaceutical interventions (NPIs) were implemented during the vaccination campaign (Table 2). The vaccination campaign started during an increase in the number of SARS-CoV-2 cases, which resulted in lockdown on 27 December 2020 and its enhancement on 8 January 2021. As the increase in the number of cases was halted, a gradual lifting of limitations occurred over time. By 18 May 2021, several limitations were still in place (Table 2).

DISCUSSION

By 18 May 2021, only 19 new SARS-CoV-2 cases were identified in Israel. Our study suggests that indirect protection against SARS-CoV-2 was achieved by that point, as the number of new cases reached a very low level despite the fact that 36.4% of the population were not vaccinated, nor had a documented past SARS-CoV-2 infection.

Our study demonstrated that SARS-CoV-2 cases declined among unvaccinated individuals of all age groups. Furthermore, the key time points in which the SARS-CoV-2 pandemic wave shifted its course during the BNT162b2 vaccine campaign were demonstrated.

Although the role of lockdowns cannot be quantified, the first breakpoint occurred during a lockdown period, when the percentage of NAV individuals of all ages was less than 10%, indicating that vaccination alone was most probably not the primary reason for the beginning of the shift in trend.

The major decline breakpoint occurred after the lockdown ended and approximately half of the population of all ages was NAV, indicating that the vaccination campaign had a major role in the sustainable decline that started at this time point.

The exception to this was the 12–15-year and 16–18-year age groups, for which the major decline breakpoint, which occurred on 11 January 2021, was also the first breakpoint. The vaccination campaign for the 16–18-year age group started at the end of January 2021, and individuals aged 12–15 years old were vaccinated at that time only in extreme circumstances, with special MOH approval. Therefore, the early start of the sustainable decline among these age groups resulted most likely from vaccination of older individuals, with the addition of lockdown that lasted until 7 February 2021. The end of decline was observed for all ages during the month of May 2021, when the NAV coverage was 63.55% for all ages.

The degree of the indirect vaccine effect can be affected by several factors: pathogen transmissibility, vaccine efficacy, pattern of population mixing, vaccine coverage, and vaccine distribution in the population [5, 17–20].

The BNT162b2 vaccine efficacy was found to be 95% [6], thus providing this vaccine with an advantage towards reaching

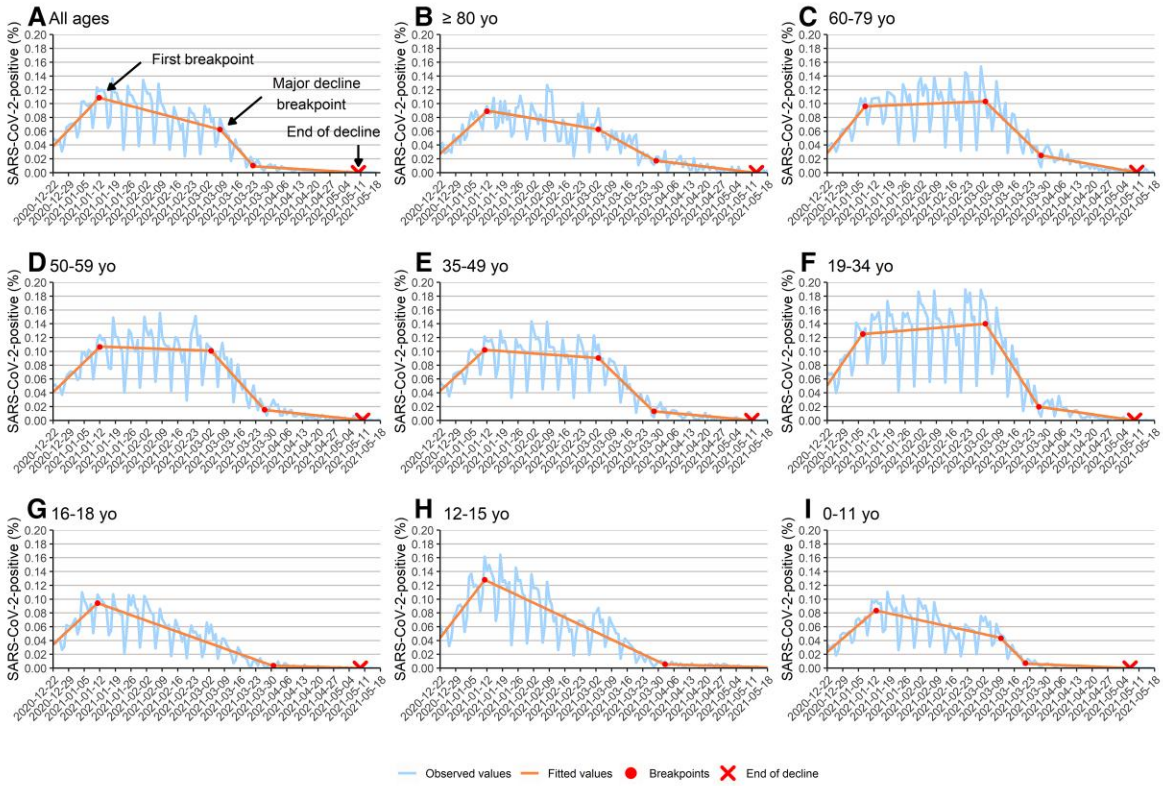

Figure 4. Piecewise regression analysis applied to the daily percentage of new PCR-confirmed SARS-CoV-2–positive cases among unvaccinated individuals of all ages (*A*) and by age group (*B–I*). The "first breakpoint," the "major decline breakpoint," and the "end of decline" are indicated in panel *A*. Abbreviations: PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; yo, years old.

indirect vaccine effect. However, waning of the BNT162b2 vaccine–induced protection against infection [21] prevented the development of longstanding herd protection and led into the Delta (B.1.617.2) variant wave that started in Israel at the end of June 2021 [12, 13, 21, 22]. A fresh BNT162b2 vaccine and a booster were found to be highly effective [10, 23, 24].

Transmissibility can vary among different SARS-CoV-2 variants [25–27]. In this regard, the Omicron (B.1.1.529) variant, which was found to have increased transmissibility as compared with previous variants, was first detected in Israel at the end of November 2021 [28]. It quickly became the predominant variant, reaching more than 90% of circulating SARS-CoV-2 viruses by 10 January 2022 [11]. Recent evaluations suggested a decreased BNT162b2 (including booster) VE against the Omicron variant [29, 30], thus affecting the potential to achieve vaccine indirect protection.

Pathogen transmissibility can also be affected by the use of NPIs, such as social-distancing measures and the use of facial masks [26]. In this regard, the early stages of the vaccine campaign took place while lockdown was in effect. Furthermore, social distancing to various degrees was in effect in Israel until 31 May 2021, and the use of masks in closed spaces was in effect until 15 June 2021. Therefore, it is possible that the indirect protection achieved in Israel was aided by the use of NPIs.

Basic mathematical models of pathogen transmission assume that populations mix homogeneously, and that disease transmission between any 2 individuals is equally probable, irrespective of their age, their residence or work location, their activity level, or other behavior characteristics [31]. However, more recent pathogen transmission models take into consideration the heterogeneous mixing patterns of populations [31]. In this regard, children are likely to have closer physical contact with their parents than other adults, and their ability to develop indirect protection can be strongly affected by their parents' vaccination status [32]. Therefore, some of the decline in SARS-CoV-2 cases among Israeli children could have been driven by their parents' vaccination status.

Our study has several limitations. As this study addressed the development of indirect protection of the Israeli population, it did not address indirect protection in subpopulations other than by age group. A study in 177 communities in Israel during the first SARS-CoV-2 wave in which a vaccine was available for individuals aged 16 years and older found that an increase in vaccination rates in these communities was associated with a

Table 1. Calculation of the Percentage of Naturally and Actively Vaccinated Individuals in the Population and by Age Group at Time Points of Interest: Israel, December 2020–May 2021

Age Group (Years)	Date	Second-Dose Coverage, t-7 Days (%)	First-Dose Coverage, t-14 Days (%)	SARS-CoV-2+ by PCR, t-14 Days (%)	NAV (%)
First breakpoint					
All ages	12 January 2021	0.00	7.26	4.53	8.16
≥80	12 January 2021	0.00	28.08	3.37	17.41
60–79	8 January 2021	0.00	12.87	3.30	9.73
50–59	12 January 2021	0.00	8.27	4.83	8.96
35–49	11 January 2021	0.00	3.63	4.75	6.56
19–34	7 January 2021	0.00	0.72	6.29	6.65
16–18	11 January 2021	0.00	0.18	4.75	4.84
12–15[a]	11 January 2021	0.00	0.00	4.87	4.87
0–11	13 January 2021	0.00	0.00	2.83	2.83
Major decline breakpoint					
All ages	8 March 2021	37.03	13.49	8.27	52.05
≥80	3 March 2021	76.68	5.11	5.58	84.82
60–79	3 March 2021	80.01	6.01	5.42	88.44
50–59	3 March 2021	63.73	12.81	7.94	78.07
35–49	3 March 2021	48.71	22.03	8.30	68.02
19–34	3 March 2021	27.98	29.94	11.57	54.52
16–18	11 January 2021	0.00	0.18	4.75	4.84
12–15[a]	11 January 2021	0.00	0.00	4.87	4.87
0–11	10 March 2021	0.00	0.00	6.38	6.38
End of decline					
All ages	10 May 2021	54.01	0.77	9.16	63.55
≥80	13 May 2021	85.01	0.50	6.02	91.28
60–79	10 May 2021	89.41	0.48	5.84	95.49
50–59	10 May 2021	81.65	0.65	8.63	90.60
35–49	11 May 2021	75.52	0.86	9.24	85.19
19–34	9 May 2021	74.13	1.88	12.91	87.98
16–18	9 May 2021	46.16	1.76	8.95	55.99
12–15[a]	After 18 May 2021	_	_	_	_
0–11	7 May 2021	0.00	0.00	7.44	7.44

Abbreviations: FDA, Food and Drug Administration; NAV, naturally and actively vaccinated; PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a]In rare cases, individuals aged 12–15 years received the BNT162b2 vaccine prior to FDA approval for this age group. These individuals received the vaccine due to the presence of underlying diseases or due to being household members of immunocompromised patients. Special approvals for their vaccination were granted on a case-by-case basis.

Table 2. Timeline of Nonpharmaceutical Interventions During the COVID-19 Vaccination Campaign: Israel, December 2020–June 2021

Milestone	Date	Main Directives
Start of vaccination campaign	20 December 2020	…
Initial lockdown	27 December 2020	1000-meter mobility limit, gathering restrictions; private sector workplace attendance at 50% capacity (except for essential workers); schools remained open (except for grades 5–10)
Enhanced lockdown	8 January 2021	Addition of school closure (except for special education and no re-entry boarding schools), no workplace attendance (except for essential workers), enhanced gathering restrictions
Stage 1 reopening	7 February 2021	Mobility limit lifted
Stage 2 reopening	21 February 2021	Beginning of nonessential commerce and activities for the public, under the "green pass" (entry for fully vaccinated and recovered individuals) regulations; gradual school reopening
Stage 3 reopening	7 March 2021	Additional school reopening; additional nonessential commerce reopening
Stage 4 reopening	19 March 2021	5000 people allowed in open sports events; children allowed in open swimming pools
Stage 5 reopening	18 April 2021	No obligation to wear masks in outdoors except for gathering
Stage 6 reopening	27 May 2021	Movie theaters re-open
Stage 7 reopening	1 June 2021	"Green pass" and "purple pass" (social-distancing guidelines indoors) use cancelled
Stage 8 reopening	15 June 2021	No obligation to wear masks in closed spaces, except for medical facilities, nursing homes, and airplanes

Abbreviation: COVID-19, coronavirus disease 2019.

decline in infection rates among individuals aged less than 16 years old [33]. However, that study did not take into account the natural immunity (which resulted from SARS-CoV-2 exposure) in these communities, nor did it establish the vaccination coverage required to reach the end of SARS-CoV-2 cases decline [33]. A study from Spain suggested the development of indirect protection against SARS-CoV-2 in unvaccinated residents of long-term-care facilities [34]. Both studies were published before waning vaccine protection became evident.

An additional limitation stems from the fact that, despite our efforts, the actual number of individuals who were infected with SARS-CoV-2 and who developed natural immunity from SARS-CoV-2 exposure is unknown and largely depends on the motivation to perform PCR testing, which may vary considerably among individuals. Two serological surveys from Israel showed that immunoglobulin G (IgG) antibodies against the SARS-CoV-2 receptor binding domain were detected among 7.7% and 8.1% of samples from individuals aged 0–15 years and 16 years and older, respectively, in the month of December 2020 [35, 36], while 4.2% of Israeli residents of all ages were SARS-CoV-2 PCR–positive on day 1 of our study. Thus, our calculation of the percentage of NAV individuals required to achieve indirect protection may be an underestimation.

In conclusion, indirect protection against SARS-CoV-2 was provided by the BNT162b2 vaccine and helped end the Alpha variant wave. However, the level of natural and active vaccination required to achieve indirect protection depends on a combination of factors, including NPI use, circulating variants, and waning immunity.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Author contributions. A. G. -F. conceived and designed the study, led data analysis, and wrote the first draft of the manuscript. M. B. oversaw the study design and analysis. Y. H. and R. D. retrieved the data. Y. H., S. F. F., Z. K., and R. D. performed data analysis. A. G. -F., S. F. F., L. K.-B., and M. B. interpreted the data and edited the final manuscript. Y. H. and R. D. verified the underlying data. All authors revised the manuscript critically for important intellectual content and approved the final version of the manuscript.

Financial support. None

Potential conflicts of interest. The authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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