

Patterns of covid-19 pandemic dynamics following deployment of a broad national immunization program

February 3, 2021

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Abstract

Studies on the real-life impact of the BNT162b2 vaccine, recently authorized for the prevention of coronavirus disease 2019 (COVID-19), are urgently needed. Here, we analysed the temporal dynamics of the number of new COVID-19 cases and hospitalization in Israel following a vaccination campaign initiated on December 20th, 2020. We conducted a retrospective analysis of real-world data from March 2020 to February 2021, originated from the Israeli Ministry of Health (MOH). In order to distill the effect of the vaccinations from other factors, including a third lockdown imposed in Israel on January 2021, we compared the time-dependent changes in number of COVID-19 cases and hospitalizations between (1) individuals above 60 years old eligible to receive the vaccine earlier and younger individuals (0-59 years old) and (2) cities who vaccinated early compared to late-vaccinated cities. and (3) the current lockdown versus the previous lockdown, imposed on September 2020. By February 2nd 2021, 42.8% and 27.6% of the entire Israeli population (88.9% and 77.7% of individuals older than 60 years old) received the first dose or both doses of the vaccine, respectively, or recovered from COVID-19. In mid-January, the number of COVID-19 cases and hospitalization started to decrease, with a larger and earlier decrease among older individuals. This trend was more evident in early-vaccinated compared to late-vaccinated cities. Such a pattern was not observed in the previous lockdown. Our analysis demonstrates early signs for the real-life effectiveness of a national vaccination campaign in Israel on the pandemic dynamics. Although our findings are preliminary, we decided to publish them as they have major public health implications in the struggle against the COVID-19 pandemic. More studies aimed at assessing the effectiveness of vaccination both on the individual and on the population level, with larger followup are needed.

Introduction

An effective and safe vaccine is urgently needed to halt the rapid spread of *Severe acute respiratory syndrome coronavirus 2* (SARS-CoV-2) infections and the resulting disease, coronavirus disease 2019 (Covid-19). The BNT162b2 vaccine, developed by BioNTech in cooperation with Pfizer, is a lipid nucleoside-modified RNA (modRNA) encoding the SARS-CoV-2 full-length spike ¹. On December 11, 2020, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for emergency use of the vaccine for the prevention of COVID-19 ². Results from a phase III randomized placebo-controlled RCT demonstrated that a two-dose regimen in a 21 days interval conferred 95% protection against Covid-19 in individuals 16 years of age or older ³.

On December 20th, Israel launched its COVID-19 vaccination campaign ⁴, and started administering BNT162b2 vaccines. In the early phases of the distribution process, individuals considered as being at high risk for COVID-19 were given a priority in vaccination, including individuals older than 60 years old, nursing home residents, healthcare workers, and patients with severe comorbidities. While up to the 21st of January vaccine prioritization rollout was mainly by age, following that date pupils aged 16-18 years old were also prioritized for vaccination. On the 28th of January, the vaccination campaign expanded for those aged 35 and older ⁵. Individuals with a history of severe allergic reactions to the vaccine components, recovered COVID-19 patients or those younger than 16 years of age (with the exception of children with severe chronic diseases) are not currently eligible to receive the vaccine (as of 2nd of February).

The national vaccination campaign has led Israel to be the country with the highest rate of vaccinated individuals per capita, with 42.8% and 27.6% of the population received the first or second vaccine dose, respectively, or recovered from COVID-19, to date (February 2, 2021). In parallel, during the early weeks of the vaccination campaign the number of cases and hospitalized patients has rapidly increased, along with the emergence of the B117 variant ⁶, leading the government to impose a third lockdown on 8th of January 2021.

Assessing the real-life effect of the vaccines, in order to show that the high efficacy observed under ideal clinical trial conditions is also seen in routine care, is of highly importance. This can be analysed by either assessing the real-life impact of vaccination programmes at a population level (termed “vaccine impact” (VI)) or by assessing the direct protective effect of the vaccine at the individual level (termed “vaccine effectiveness” (VE)) ⁷. On the individual level, a first report from one of the largest Israeli health maintenance organizations (HMO's) concluded an effectiveness of 51% for the first dose of BNT162b2 vaccine after 13-24 days in a real-life setting ⁸. However, to our knowledge, no study thus far has studied the impact of the vaccination campaign on the population level and its effect on the patterns of pandemic dynamics. As Israel

is one of the first countries to implement a vaccination campaign on this magnitude, we believe that this quantification may be of major interest for many countries worldwide.

Methods

We conducted a retrospective analysis on data from March 2020 to February 2021, originated from the the Israeli Ministry of Health (MOH) that included information on age, sex, date of positive SARS-CoV-2 polymerase chain reaction (PCR) test, date of hospitalization, state of hospitalization and date of death for each individual. Data on vaccination is available online for daily doses administered at the resolution of towns and age groups (resolution of 10 years) (<http://data.gov.il/dataset/covid-19/>).

In order to assess the real life effectiveness of the vaccine on the national level, we made the following comparisons: First, we compared between individuals aged 0-59 years old and those 60 years and older, who were prioritized to receive the vaccine earlier. Second, we compared between cities in which there was a high percentage of individuals who were vaccinated early, annotated here as early vaccinated cities, to cities with a low percentage, annotated here as late vaccinated cities. To that end, for each city in which more than 5,000 individuals older than 60 years old reside, we calculated the percentage of these individuals who received the first dose of the vaccine. Early vaccinated cities were considered as those with at least 85% individuals who are older than 60 years old were either vaccinated or recovered, while late vaccinated cities were considered as those with less than 70% vaccinated by the 10th of January 2021 (see Fig. S4).

For each of these comparisons, we analysed the temporal changes in weekly numbers of positive COVID-19 cases, hospitalized patients, hospitalized patients in a moderate and severe state, and hospitalized patients in a severe state. Covid-19 cases were identified by a positive SARS-CoV-2 polymerase chain reaction (PCR) test. Classification of the hospitalization severity was based on the following clinical criteria, applied on 13 of July 2020 by the Israeli MOH⁹ based on NIH¹⁰ and WHO¹¹ definitions: *Mild illness* - individuals who have any of the various signs and symptoms of COVID 19 (e.g., fever, cough, malaise, loss of taste and smell); *Moderate illness* - individuals who have evidence of pneumonia by a clinical assessment or imaging; *Severe illness* - individuals who have respiratory rate >30 breaths per minute, SpO₂ <93% on room air at sea level, or ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO₂/FiO₂) <300 mmHg and *Ventilated/Critical* - individuals with respiratory failure who require ventilation (invasive or non-invasive), multiorgan dysfunction or shock. In our analyses here, we denote all patients in a severe case or worse as severe (including ventilated and critical patients).

Results

We first analysed the number of COVID-19 cases and the percentage of vaccinated individuals in Israel. Starting on the 20th of December 2020, the initiation of the vaccination campaign, the number of vaccines administered per day began at approximately 50,000, quickly rose to over 150,000 by December 24th 2020, and reached a maximum of 229,508 on January 21st 2021 (Fig

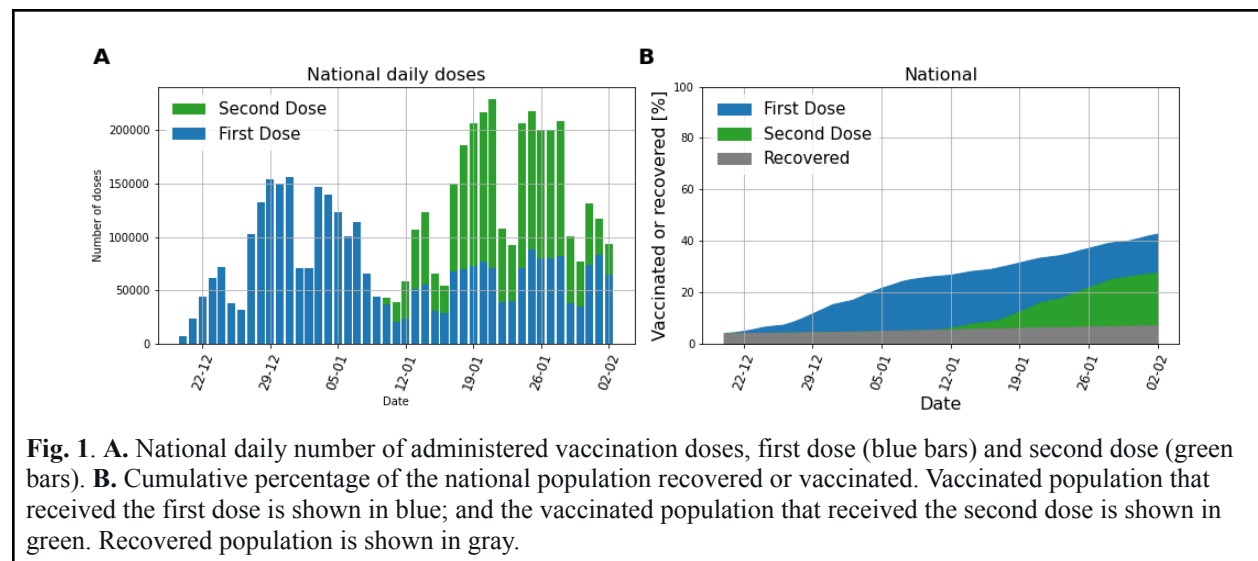
1). Vaccination per day for each age group is shown at the appendix (Fig S1). By January 7th, 75% of the population over 60 years old have already been vaccinated (1st dose) or recovered, increasing gradually to 88.9% (1st dose) and 77.7% (both doses) by February 2nd 2021.

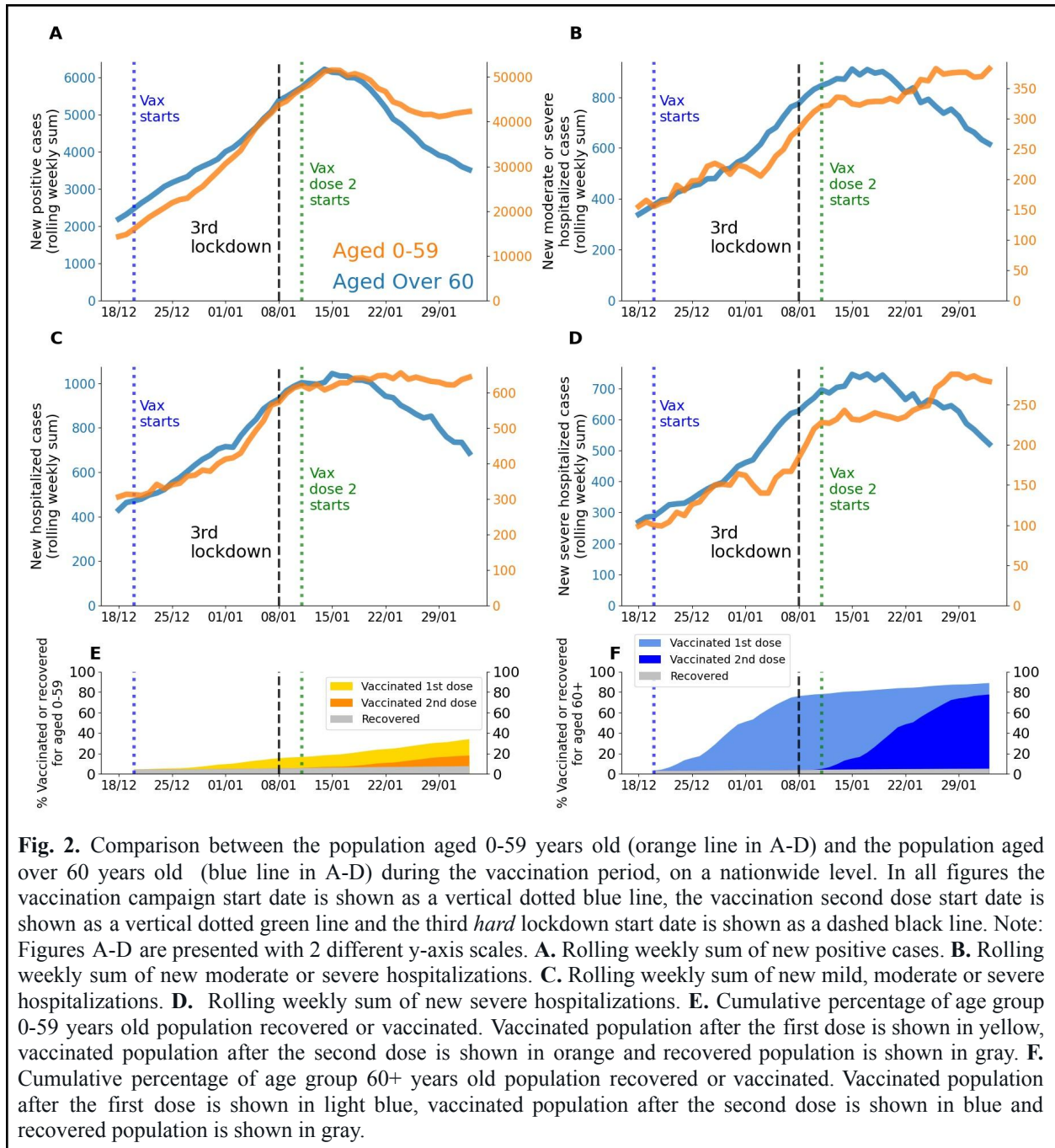
We next analysed the temporal changes in the number of new COVID-19 cases and hospitalization in Israel from December 18th to February 2nd. In order to distill the effect of the vaccination from other factors that might have influenced the decrease in the number of new cases and hospitalization such as the lockdown, we performed the following comparisons:

First, we compared between individuals aged 0-59 years old and individuals 60 years and older, who were prioritized to receive the vaccine earlier. Notably, the decrease in number of cases and hospitalizations was larger and earlier in older individuals compared to younger individuals, who were only recently eligible to receive the vaccine.

Second, we compared between *early* vaccinated cities and *late* vaccinated cities (see Methods). This analysis revealed a larger and earlier decrease in the number of COVID-19 cases and hospitalizations of individuals 60 years old in cities vaccinated early compared to late-vaccinated cities

Finally, we compared between the decrease in number of cases and hospitalizations observed following the second national lockdown imposed by the Israeli government on 18th of September 2020, and the dynamics observed following the third national lockdown, imposed on the 8th of January 2021. The larger decline in older individuals (age above 60 years old) compared to younger individuals (0-59 years old) was only apparent in the third lockdown.





Group	Age group, years	% change from		
		14 days back	21 days back	28 days back
New cases	0-59	-15.7	-12.3	9.6
New cases	60+	-40.1	-40.5	-24.4
New Hospitalizations:				
Mild, Moderate or Severe	0-59	0.3	5.4	30.4
Mild, Moderate or Severe	60+	-32.3	-31.3	-18
Moderate or Severe	0-59	16.5	18.6	60.5
Moderate or Severe	60+	-31.6	-28.1	-9.5
Severe	0-59	17.7	22.9	75.5
Severe	60+	-30	-24.1	-8.4

Table 1. Percent change of national COVID-19 cases and hospitalizations measures. Change is presented 14,21,28 days before February 2nd and all changes are with respect to weekly sums of national measures.

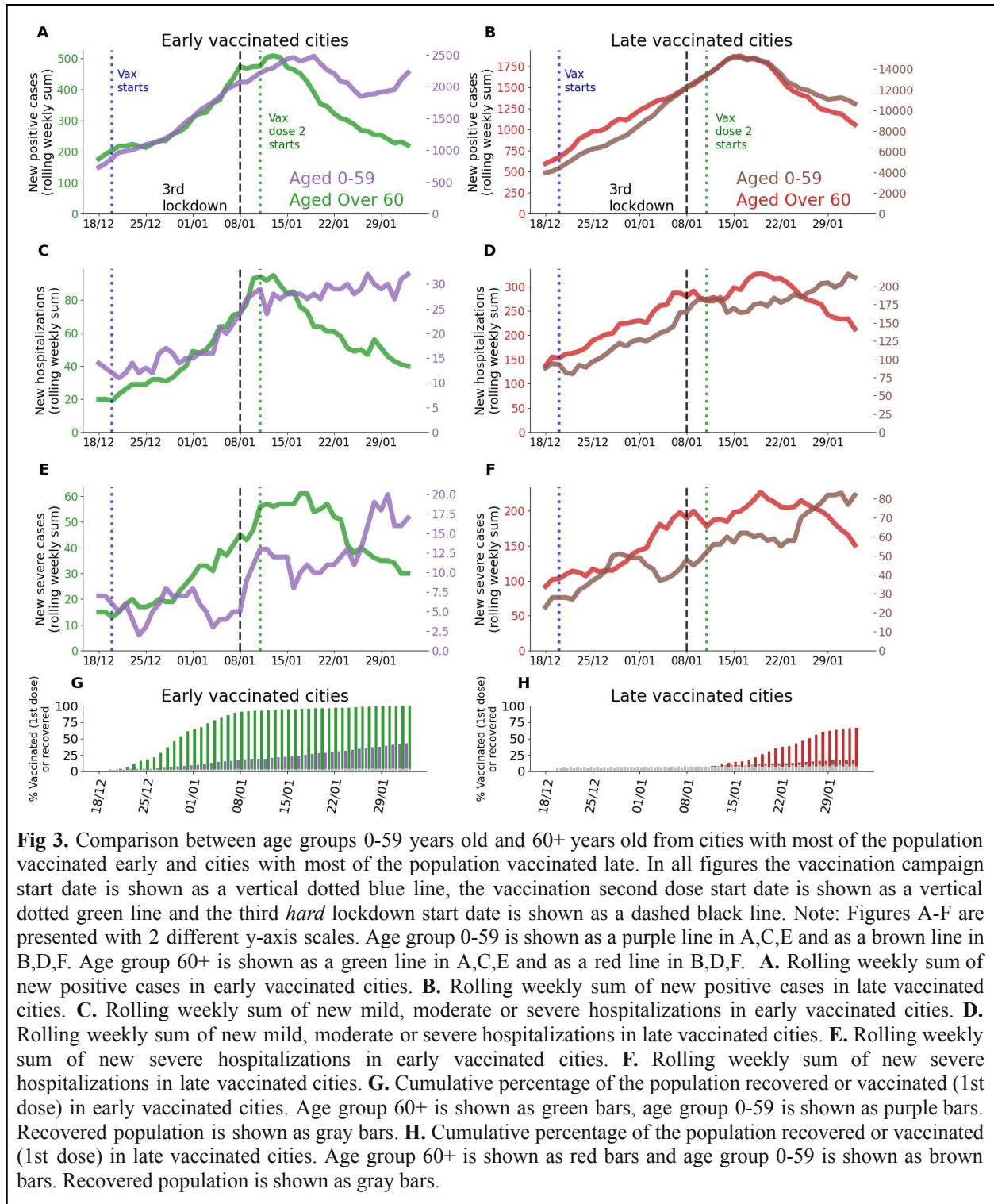


Fig 3. Comparison between age groups 0-59 years old and 60+ years old from cities with most of the population vaccinated early and cities with most of the population vaccinated late. In all figures the vaccination campaign start date is shown as a vertical dotted blue line, the vaccination second dose start date is shown as a vertical dotted green line and the third *hard* lockdown start date is shown as a dashed black line. Note: Figures A-F are presented with 2 different y-axis scales. Age group 0-59 is shown as a purple line in A,C,E and as a brown line in B,D,F. Age group 60+ is shown as a green line in A,C,E and as a red line in B,D,F. **A.** Rolling weekly sum of new positive cases in early vaccinated cities. **B.** Rolling weekly sum of new positive cases in late vaccinated cities. **C.** Rolling weekly sum of new mild, moderate or severe hospitalizations in early vaccinated cities. **D.** Rolling weekly sum of new mild, moderate or severe hospitalizations in late vaccinated cities. **E.** Rolling weekly sum of new severe hospitalizations in early vaccinated cities. **F.** Rolling weekly sum of new severe hospitalizations in late vaccinated cities. **G.** Cumulative percentage of the population recovered or vaccinated (1st dose) in early vaccinated cities. Age group 60+ is shown as green bars, age group 0-59 is shown as purple bars. Recovered population is shown as gray bars. **H.** Cumulative percentage of the population recovered or vaccinated (1st dose) in late vaccinated cities. Age group 60+ is shown as red bars and age group 0-59 is shown as brown bars. Recovered population is shown as gray bars.

Group	Age group, years	% change from					
		14 days back		21 days back		28 days back	
		Early cities	Late cities	Early cities	Late cities	Early cities	Late cities
New cases	0-59	-10.4	-28.1	-1.9	-23.2	20.6	-1.3
New cases	60+	-43.6	-41.6	-56.3	-37.8	-39.9	-22.4
New Hospitalizations:							
Mild, Moderate or Severe	0-59	14.3	19.8	33.3	17.8	52.4	52.5
Mild, Moderate or Severe	60+	-37.5	-34.9	-56.5	-23.4	-37.5	-19
Severe	0-59	70	34.4	30.8	46.4	325	115.8
Severe	60+	-44.4	-33.5	-47.4	-19.3	-23.1	-13.7

Table 2. Percent change of COVID-19 cases and hospitalizations measures for early and late vaccinated cities. Change is presented 14,21,28 days before February 2nd and all changes are with respect to weekly sums of national measures.

Discussion

Here we show early signs for the real-life effectiveness of a national vaccination campaign in Israel on the pandemic dynamics. Our analysis revealed that in the past week, approximately one and a half month after the initiation of the vaccination campaign, with 77.7% of individuals older than 60 years old already vaccinated (February 2nd 2021), there was an approximately 41% drop in number of cases, 31% drop in COVID-19 related hospitalizations and 24% drop in critically ill patients compared to 21 days ago. Although multiple other factors may have influenced these results, several observations suggest that these patterns are driven to a considerable degree by the vaccines. First, the decline in the measures above is greater in older individuals who were prioritized to receive the vaccine earlier. Second, the effect was greater in cities where a higher fraction of individuals were vaccinated. Finally, we did not observe similar dynamics in the previous lockdown imposed in Israel (Supp. Figs S3. & S5).

Notably, although previous reports have indicated that efficacy of the vaccine, is already evident after the first dose ^{3,8}, the improvement in the number of new cases and hospitalized patients has occurred only 21 following the vaccination campaign. We believe that this has several reasons. First, the effect of vaccines in real-life may take longer than demonstrated in clinical trials due to numerous reasons. For example, the logistics of refrigeration, storage, transportation and on-site administration of the vaccines in real life and during a rapid deployment campaign may have been imperfect, thus lowering effectiveness. Second, the effect may be heterogeneous and population-dependent. For example, it is possible that older individuals, who were prioritized

earlier in the vaccination campaign, may have a reduced or belated response to the vaccination due to a deterioration in both innate and adaptive immune function, also termed immunosenescence, as was previously shown for other vaccinations ^{12,13}. Third, it is possible that the efficacy of the vaccine is reduced in light of the emergence of new and more violent viral strains, such as the B117 variant ¹⁴ (which is already prevalent in Israel at February 2021 according to the Israeli MOH), and the South African variant ¹⁵ which may be associated with an increased risk of death ¹⁶. Fourth, it is possible that vaccinated individuals may alter their behaviour and decrease adherence to public health prevention guidance (e.g. physical distancing, face masks) thereby increasing viral transmission. Moreover, viral transmission may also occur in the vaccination areas themselves. The vaccination sites should be large and ventilated in order to decrease the probability of transmission on site. Finally, there is a clear trend where areas in Israel with higher infection rates and a lower socioeconomic status have lower vaccination rates, despite wide vaccination availability ¹⁷. Further effort should be made to encourage these populations to vaccinate and make the vaccines even more easily accessible for them. We note that exact efficacy numbers cannot be deduced from our analysis, and that due to all of the above issues, our results may be consistent with efficacies that are either lower or greater than those reported in the original clinical trial.

Our study has several limitations. First and foremost, our study is an observational study as opposed to a randomized clinical trial and therefore causal effects are difficult to infer. Second, the comparison between the second and third lockdown may be influenced by factors such as the total number of COVID-19 cases in the beginning of each lockdown, testing policy, hospitalization policy and public compliance to the restrictions that may have changed with time. Similarly, differences between cities might be influenced by behavioral and social differences beyond the vaccines. However, none of these factors were likely to cause the different patterns observed in the different age groups reported here. Finally, the effects of the vaccination campaign observed here may be influenced by factors specific to Israel and its healthcare system, in which all citizens are mandated to join one of the official non-profit health insurance organizations. Financial and regional disparities in other health-care systems may impact the distribution and availability of vaccinations, thereby influencing the real life efficacy of the vaccines.

In conclusion, here we show an analysis of large-scale real-world data from Israel demonstrating first signs of real-life effectiveness of a national vaccination campaign. Although our findings are preliminary, they have major public health implications for the struggle against the COVID-19 pandemic. More studies aimed at assessing the effectiveness of the vaccination on reducing the transmission of SARS-CoV-2 are needed both on the individual and on the population level with larger longitudinal followup and in additional populations.

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Data availability statement

The data that support the findings of this study originates from the Israel ministry of health.

Aggregated town-level and age groups vaccination data is available at:

<https://data.gov.il/dataset/covid-19/resource/12c9045c-1bf4-478a-a9e1-1e876cc2e182>

National age-group level vaccination data:

<https://data.gov.il/dataset/covid-19/resource/57410611-936c-49a6-ac3c-838171055b1f>

Some restrictions apply to the availability of parts of the data used in the analysis and so are not publicly available.

Code availability statement

Any relevant source code will be made available at:

<https://github.com/hrossman/Patterns-of-covid-19-pandemic-dynamics-following-deployment-of-a-broad-national-immunization-program>

Ethics Declarations

An exemption from institutional review board approval was determined by the Israeli Ministry of Health as part of an active epidemiological investigation, based on use of anonymous data only and no medical intervention.

Competing Interests Statement

The authors declare no competing interests.

Authors contribution

H.R conceived the project, designed and conducted the analyses, interpreted the results and wrote the manuscript; S.S & T. M designed and conducted the analyses, interpreted the results and wrote the manuscript; M.G, U.S, E.S designed the analyses, interpreted the results, wrote the manuscript, supervised and conceived the project.

Supplementary appendix

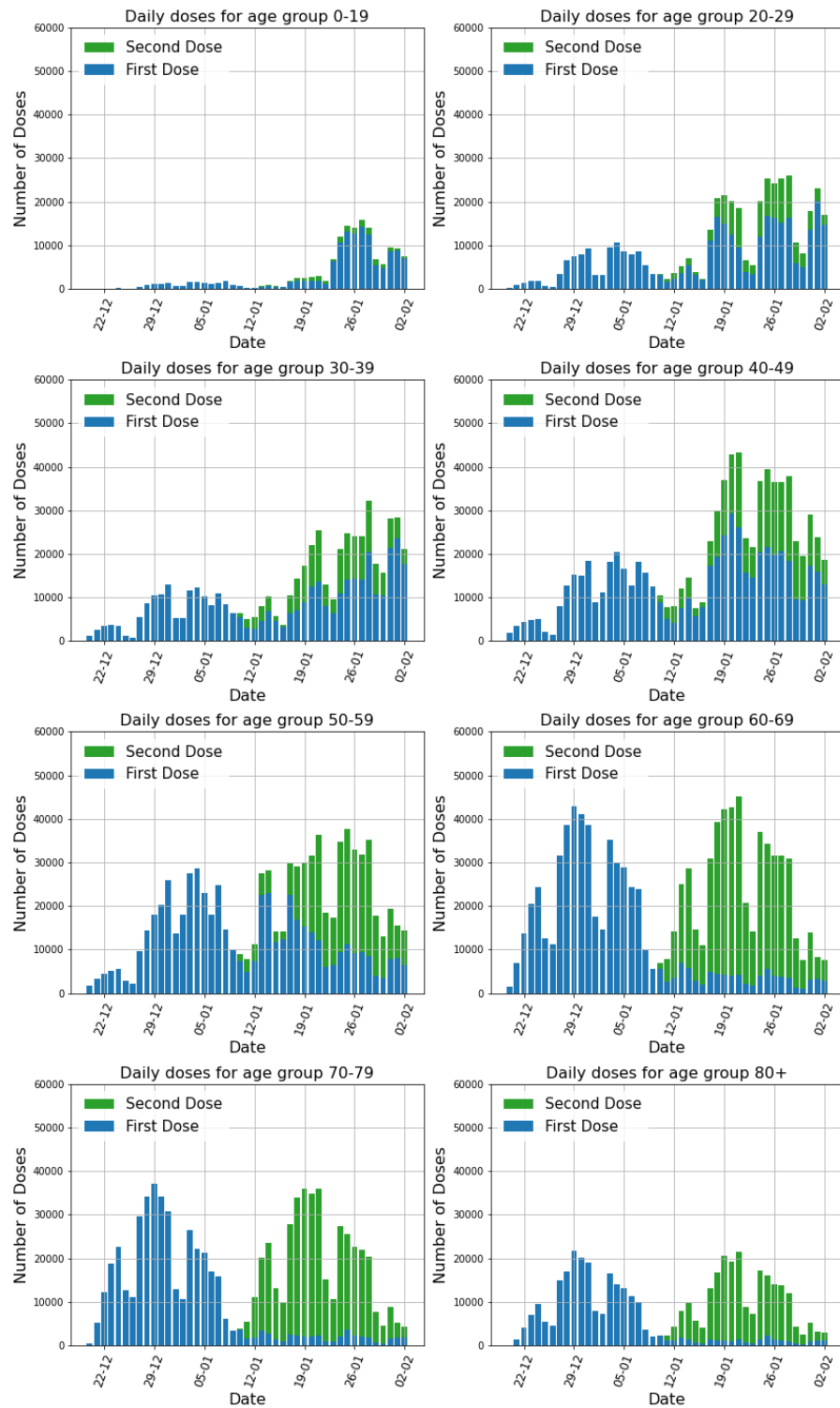


Fig S1. Daily number of administered vaccination doses for each age-group, first dose (blue bars) and second dose (green bars).

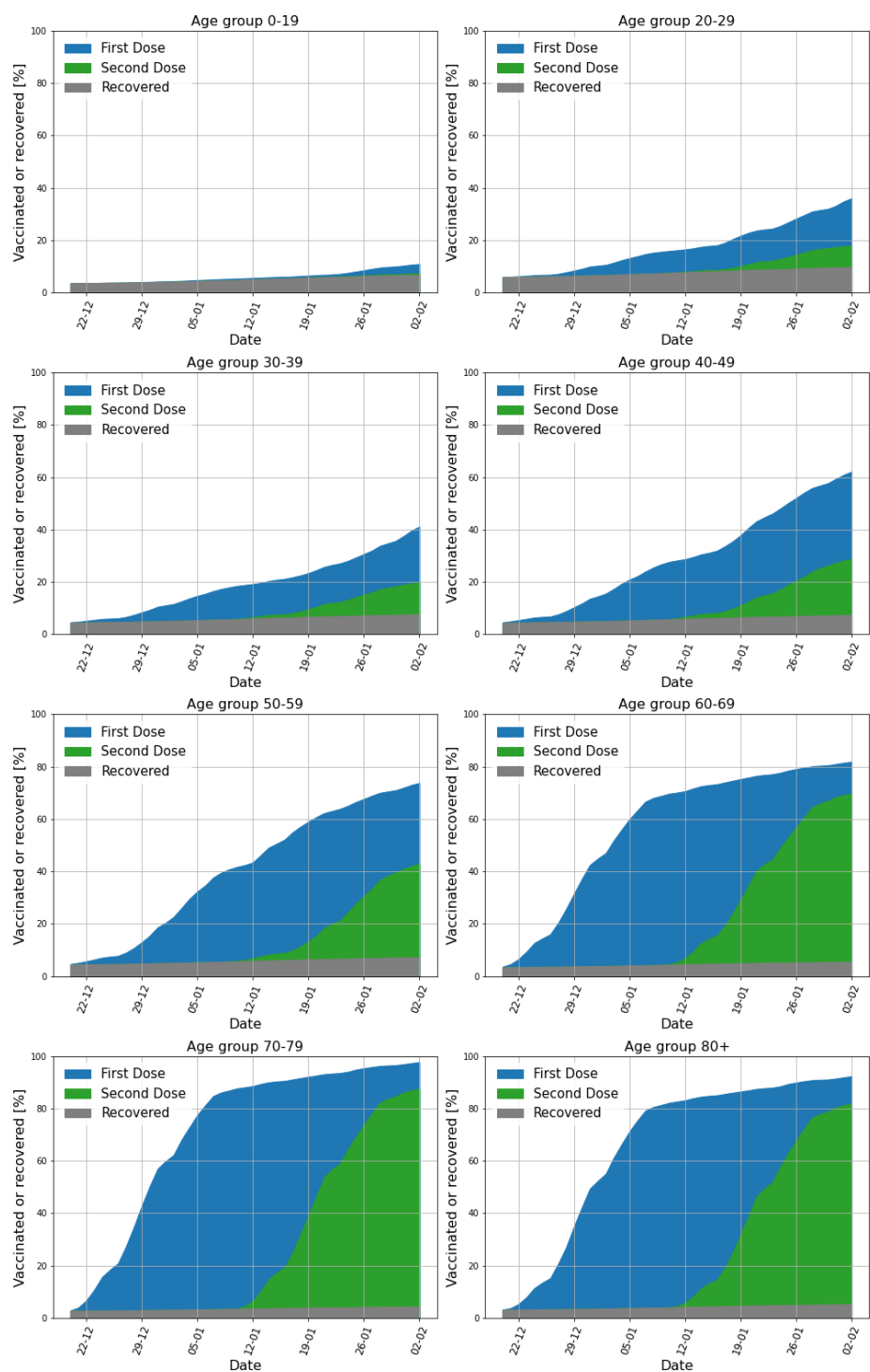


Fig S2. Cumulative percentage of each age-group population recovered or vaccinated. Vaccinated population that received the first dose is shown in blue; and the vaccinated population that received the second dose is shown in green. Recovered population is shown in gray.

