The effects of rapid mass vaccination against SARS-CoV-2 and its Variants-of-Concern: Evidence from an early VoCs hotspot

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The effects of rapid mass vaccination against SARS-CoV-2 and its Variants-of-Concern: Evidence from an early VoCs hotspot

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We studied the real-life effect of an unprecedented rapid mass vaccination campaign. Following a large outbreak of B.1.351 and B.1.1.7/E484K in the district of Schwaz/Austria, 100,000 BNT162b2 doses were procured to mass vaccinate the entire adult population (16+) of the district between the 11th and 16th of March 2021. This made the district the first widely inoculated region in Europe. We examined the effect of this unique campaign on the number of infections including VoCs, hospital and intensive care unit (ICU) admissions. We compared Schwaz with (i) a control group of highly similar districts, and (ii) with populations residing in municipalities along the border of Schwaz which were just excluded from the campaign. We find large and significant decreases for all outcomes after the campaign, including VoCs cases. The reduction relative to the control regions was largest for younger age cohorts, which were mostly non-vaccinated in the rest of the country due to the age-gradient in the national vaccination plan. Our results demonstrate that rapid population-wide mass vaccination can be an effective tool to curb overall infections as well as VoCs.

Introduction

In the autumn of 2020, the emergence of SARS-CoV-2 variants of concern (VoCs, mostly B.1.1.7 and B.1.351) was detected in Europe and elsewhere (1-3). By spring 2021, one of the largest outbreaks of B.1.351 and B.1.1.7/E484K in Europe occurred in the district of Schwaz, Austria (4). A main concern was that the mutations that these variants carry in their spike protein may make them less susceptible to the immune response induced by vaccines. In response to this local outbreak, the Government of Austria and BioNTech joined forces in an effort to supply 100,000 extra vaccine doses of BNT162b2 to rapidly mass vaccinate the entire adult population (16+) of Schwaz. Between 11th and 16th of March, more than 70% of the adult population of Schwaz received their first dose of BNT162b2, which made Schwaz the first widely inoculated region in Europe. This stood in sharp contrast to the slow vaccination progress of the rest of the country, which had a vaccination coverage (first dose) of 10% at that time. Thus, this local mass vaccination campaign created stark differences in vaccine coverage at the district level of otherwise highly integrated regions with very similar spread of SARS-CoV-2 prior to the campaign. We exploit this stark difference in local vaccine coverage to study differences in the number of infections, circulation of VoCs, hospitalizations and intensive care unit (ICU) admissions following this mass vaccination campaign. This local, population-wide mass vaccination event provides a unique opportunity to study the impact of rapid vaccination campaigns against SARS-CoV-2 and its VoCs.

Previous evidence from real-world coronavirus disease 2019 (COVID-19) vaccination campaigns is mostly based on the comparison of groups which were prioritized in national vaccination plans (e.g., elderly people, or individuals with medical conditions at risk of COVID-19) with unvaccinated controls (5-9). Prioritization in the national vaccination plans are not random but often based on multi-tiered selection criteria such as age, medical condition or socioeconomic status, which may make comparisons challenging. Another approach to quantify the impact of real-world COVID-19 vaccinations is to measure the overall effect of the vaccination program on an entire population (10). In the district of Schwaz, the entire adult population was offered vaccination (and administered within 5 days), regardless of their age or any other factors. It is this population-wide rapid mass vaccination which sets our study apart. It allows us to compare outcomes of a general population living within the same geographical area but across district borders, resulting in very different vaccine coverage. Our study design keeps confounding factors such as the healthcare system, local conditions facilitating the spread of SARS-CoV-2, and general population characteristics as constant as possible. Finally, due to the occurrence of B.1.351 and B.1.1.7 E484K at significant numbers in the district of Schwaz,

our study provides novel evidence of the real-life effect of the vaccine on an entire population regarding two of the most common VoCs.

Methods

Data sources used

For our retrospective observational study we used data from the Austrian epidemiological reporting system (Österreichisches Epidemiologisches Meldesystem, EMS). These data are collected by the Austrian National Public Health Institute (Gesundheit Österreich GmbH, GÖG), along with information on hospital admissions due to COVID-19 diagnosis. Our database comprises municipality/district-level epidemiological datasets of laboratory testing, sequencing (VoCs), and hospital/ICU admission data. Sequencing data is only available for the state of Tyrol, which responded with comprehensive sequencing of almost all SARS-CoV-2 PCR-positive cases after the large outbreaks of B.1.351 and B.1.1.7/E484K. Vaccination data ("e-Impfpass") is only available for the state of Tyrol, since the federal states are responsible for the roll-out of the national vaccination plan. Our sample selection is based on the universe of all Austrian districts (all Tyrolian districts in the case of the vaccination and sequencing data) and all municipalities within those districts. We employed all infections, VoC cases, hospital and ICU admissions recorded for those geographical units.

Study design and statistical analysis

Our study design exploited the fact that very similar municipalities which share many geographical as well as socio-demographic characteristics ended up with very different vaccine coverage following the mass vaccination campaign in Schwaz in March (dose 1) and April (dose 2) 2021. To distinguish the possible effects of the vaccination on (variant) cases and hospitalizations from other factors, we used two different methods providing alternative comparisons of post-campaign virus transmission:

First, we used the *synthetic control method* (SC), which is widely applied in causal analysis (11-13), and also in recent health and Covid-19 research (14, 15). The synthetic control group is constructed through a data-driven process in which weights are assigned to a donor pool of all 91 Austrian districts to approximate as closely as possible the pre-treatment characteristics of Schwaz. The choice of the weights is based on the SARS-CoV-2 infection spread prior to the vaccination campaign and additional covariates such as population size, geographical area size and the number of municipalities within a district (see also Supplementary **Table A1** which summarizes further details on the profiles of Schwaz and the synthetic control group). Once the treatment took place (i.e., roll-out of the first dose in the campaign), the respective outcome variable is compared between Schwaz and its synthetic counterpart. This allows to estimate what would have happened to Schwaz in the absence of the mass vaccination campaign. To evaluate the significance of the differences observed between Schwaz and the synthetic control group, we employed a standard permutation test (13,15).

Second, we made use of our very fine-grained geographical data to compare adjacent municipalities just within versus just outside the district of Schwaz before and after the roll-out of the first dose. We selected those border municipalities on the basis of road connectivity to the district of Schwaz. Specifically, we only selected border municipalities outside the district of Schwaz as control units when there existed a direct road link between the respective border municipality and Schwaz. This ensures that the populations living in these border municipalities share many geographical and socio-demographic characteristics (e.g., local mobility) with Schwaz but were excluded from the mass vaccination campaign. We employed an event-study model based on a *difference-in-difference* (DID) design to measure the impact of the campaign

in Schwaz relative to the border municipalities (13,16). Empirically, we estimated a two-way fixed-effects model including an indicator variable for municipalities located in Schwaz as the treated units. We allocated our daily data into weekly periods starting from the 18th of January 2021 and calculated for each week k the DID in the 7-day moving average of new infections (per 100,000 inhabitants) between the group of bordering municipalities and Schwaz. The regression equation is given by

$$y_{it,w} = \delta_i + \delta_w + \sum_{k=-6}^{-1} \beta_k D_{it,w} + \sum_{k=1}^{16} \beta_k D_{it,w} + \epsilon_{it,w}, \quad (1)$$

where $y_{it,w}$ denotes the 7-day moving average of new infections (per 100,000) in municipality i (Schwaz or border municipalities) and day t, which is nested in week w. δ_i and δ_w denote municipality- and week-fixed effects, and $D_{it,w}$ is the treatment variable taking a value of 1 for municipalities in Schwaz and 0 for border municipalities just outside of Schwaz. k in the sum operators indicate leads (first sum) and lags (second sum) of the treatment effect. $\varepsilon_{it,w}$ is the error term. Standard errors are clustered at the municipality level. Our coefficients of interest are the β_k, which measure the difference in the outcome variable (e.g., daily infections) between Schwaz and the neighboring border municipalities at a given week k relative to the omitted reference category, which is the week of the first dose of the campaign (11th to 16th of March).

Third, we calculated the overall average effect of the vaccination campaign in Schwaz relative to the neighboring border municipalities using a standard two-period DID analysis. Specifically, we estimated one post-treatment effect that comprised the average effect over all post-campaign weeks starting 14 days after the roll-out of the first dose which is approximately the time period after which first effects of BNT162b2 materialized in the original clinical trial (17). We reported the point estimate and its associated 95% CI. Standard errors are clustered at the municipality level.

Results

Impact of the mass vaccination campaign on vaccine coverage

To illustrate the stark difference in vaccine coverage following the mass vaccination campaign we calculated the shares of the adult population that received the first and second dose, respectively. **Figure 1** plots these shares for the district of Schwaz as well as for all other Tyrolian districts (pooled together). The massive impact of the mass vaccination campaign in Schwaz vis-à-vis the other districts is striking. Prior to the first dose of the campaign (11th to 16th of March), vaccination coverage of first doses was approximately 10% in Schwaz and everywhere else. After the first campaign week, vaccination coverage increased by approximately 60 percentage points to more than 70% of the adult population. When three weeks later the second dose was administered (8th to 11th of April), Schwaz became one of the regions in Europe with the highest vaccine coverage. The stark difference (especially regarding the second dose) between Schwaz and the other districts persisted over months, providing a unique setting to study the impact of the vaccine against SARS-CoV-2 and its VoCs.

Schwaz vs. synthetic control group

To examine the impact of this stark difference in vaccination coverage we used the daily number of SARS-CoV-2 infections at the district level as the respective outcome variable. We calculated the cumulative daily infections from the second week of January 2021 onwards. We employed the synthetic control group method which allowed us to estimate what would have happened to Schwaz in the absence of the mass vaccination campaign.

Figure 2 shows the cumulative daily infections per 100,000 inhabitants for Schwaz and the synthetic control group. Two observations stand out: First, **Figure 2b** shows that both the treatment and the (synthetic) control group had very similar spread of SARS-CoV-2 infections prior to the mass vaccination campaign, confirming that the two groups are highly comparable. Second, around 3-4 weeks after the first dose, the sum of infections started to diverge (**Figure 2a**). While the sum of infections in the control group continued to rise, infections in Schwaz came to an almost complete halt. Around four months after the first dose we found the cumulative daily infections per 100,000 inhabitants in the control group to be about 2,400, and 1,500 in Schwaz. We tested for the significance of this difference using a standard permutation test, which resulted in a p-value of 0.013, suggesting that the probability of observing the large treatment effect of Schwaz by pure chance is very low. Relating the observed difference of 900 (avoided) infections to the number of infections in the synthetic control group gives a reduction of 53.6%. It should be noticed that this estimate cannot be directly compared to individual-level efficacy numbers published in the original clinical trial (17). Different to a clinical trial, the impact of a vaccination program on an entire population hinges on additional factors such as vaccine coverage, vaccine uptake of subgroups, or suboptimal immune status of individuals in the population. In addition, the population in our control group is partially vaccinated as well, which again is different to the original clinical trial design (see **Figure 1**).

Next, we studied the cumulative daily infections per 100,000 inhabitants by age group. As in most other countries, Austria prioritized its national vaccination plan by age. Thus, we would expect the biggest difference of the mass vaccination campaign in Schwaz (which was rolled out independently of age) for younger age groups. **Figure 3** shows the difference in the sum of daily infections between Schwaz and the synthetic control group. As depicted in **Figure 3**, the biggest difference in the number of infections between Schwaz and the control group appeared in the youngest age groups. Unfortunately, our data does not allow to disaggregate by age for those below the age of 20, which is an age group that was only partly offered a vaccine in the campaign (16+ years). However, for the youngest age group included in our data (20-34 years) we found the largest difference of around 1,200 infections per 100,000 inhabitants between Schwaz and the control districts. In contrast, those above 80 showed the lowest difference in cumulative infections, i.e., 350 per 100,000 inhabitants. Overall, we found that the incidence by age group in Schwaz followed the age gradient of the national vaccination plan in an inverse relationship. In other words, we found the highest impact of the mass vaccination campaign in Schwaz for the age groups with lowest priority according to the national vaccination plan.

Next, we examined hospital admissions related to confirmed SARS-CoV-2 infections. For this outcome variable, we only had weekly data up to calendar week 21 available (i.e., 11 weeks after dose 1 of the campaign). **Figure 4a** shows the cumulative weekly hospital admissions per 100,000 inhabitants for Schwaz and the synthetic control group. We found that prior to the mass vaccination campaign, both the treatment and control group had very similar numbers of hospital admissions. Around 4 weeks after the first dose administered during the campaign, the number of hospital admissions started to diverge. 11 weeks after the first dose we found the cumulative weekly hospitalizations per 100,000 inhabitants was 126.8 in the synthetic control group and 71.0 in Schwaz. Relating this difference of 55.7 (avoided) hospitalizations gives a reduction in hospital admissions of about 78%.

Furthermore, we studied admission to ICUs related to a confirmed SARS-CoV-2 infection. **Figure 4b** shows the cumulative weekly ICU admissions per 100,000 inhabitants for Schwaz and the synthetic control group. We found that ICU admissions of the two groups started to diverge around 5 weeks after the first administered dose. 11 weeks after the first dose the cumulative weekly ICU admissions (per 100,000 inhabitants) was 21.8 in the synthetic control group and 16.6 in Schwaz. Relating this difference of 5.2 (avoided) ICU admissions gives a reduction of around 31%. This smaller effect on ICU compared to general hospital admissions

may be explained by the observed time-gap between infection, hospitalization, and ICU admission. Our hospitalization data ends in calendar week 21 and therefore only 7 weeks after dose 2, which might be too soon to find large effects on ICU admission. In addition, it should be noted that the ICU effect is based on small numbers, with an average of only 1.45 ICU admissions per week in the control group over the entire time period. In contrast, weekly admissions for general hospitalizations are six times higher, with an average value of about 8.45 admissions.

Schwaz vs. bordering municipalities

In addition to the analysis based on the synthetic control group, we also compared the district of Schwaz with adjacent municipalities located along the district border. Thus, this analysis examined infections among local populations residing within the same geographic area, but with stark differences in vaccine coverage after the campaign. In this analysis we also used VoC cases as additional outcome variable, since sequencing data was only available for the state of Tyrol (but not for all districts used in the synthetic control method).

Figure 5 plots the weekly treatment effects of an event-study model, capturing the difference between Schwaz and the border municipalities relative to the reference period (week of the first dose of the campaign, 11th to 16th of March).). Specifically, the figure shows the weekly coefficients β_k estimated from equation (1) with the associated 95% CI. **Figure 5a** is based on all infections as the respective outcome variable, whereas **Figure 5b** focuses only on confirmed cases of the two major VoCs (B.1.351 and B.1.1.7/E484K). Both panels of the figure show that in the weeks prior to the mass vaccination campaign, the differences between Schwaz and the border municipalities were not statistically different from zero. Starting approximately 3-4 weeks after the first dose, we found that the number of new cases in Schwaz significantly decreased relative to the border municipalities. This is true for both overall infections as well as for the VoCs, although the decrease is somewhat lower for the variant cases. For the last weeks included in our data (May/June 2021) we found the difference between Schwaz and the control group to become somewhat smaller, which is most likely due to the gradually increasing vaccine coverage also in the control municipalities.

To calculate the overall (post-treatment) effect of the vaccination campaign compared to the neighboring border municipalities, we employed a standard two-period DID analysis. Column (1) of **Table 1** is based on the 7-day moving average of all infections (per 100,000 inhabitants) as outcome variable and represents the average effect of the weekly coefficients after the vaccination campaign depicted in **Figure 5a**. 16 weeks after the roll-out of the first dose, the average post-campaign effect shows a reduction by about 15.6 in the 7-day moving average of new infections in Schwaz relative to the border municipalities. To put this number into perspective, in the 6 weeks prior the campaign the average 7-day moving average of new infections was 24.73 in Schwaz. To determine the percent reduction of new infections due to the vaccination campaign (relative to the border municipalities) we used a log-level transformation and calculated a semi-elasticity, which showed a reduction in the 7-day moving average of new infections of around 64.0% (95%-CI: -78.8% – -38.7%).

In column (2) and (3) we use confirmed cases of B.1.351 and B.1.1.7/E484K as outcome variable, respectively. We found a significant reduction of -4.4 in the 7-day moving average of new cases in B.1.1.7/E484K over all post-campaign weeks in Schwaz relative to the border municipalities. Over the 6 weeks prior to the campaign, the average 7-day moving average of new B.1.1.7/E484K cases in Schwaz was 2.87. Calculating a semi-elasticity as above gives a reduction of around 34.6% (95%-CI: -55.7% – -3.4%). For B.1.351 (column 4), we found a significant reduction of 6.1 in the 7-day moving average of new cases over all post-campaign weeks in Schwaz relative to the border municipalities. In the 6 weeks prior to the campaign, the average 7-day moving average of new B.1.351 cases was 10.57. Calculating a semi-elasticity

as above gives a reduction of 56.5% (95%-CI: -75.9% – -21.5%). For B.1.617.2 (Delta variant) we observed some cases in our control municipalities but no single case for the district of Schwaz, which prevents us from running regression analysis for this variant. In summary, we concluded that the vaccination campaign also had significant and sizable effects on major VoCs, although with a somewhat lower percent reduction. Nevertheless, our results are encouraging and suggest that mass vaccination campaigns (especially when administrating two doses within a short period of time) effectively curb the spread of the major variants.

Columns (4) and (5) are based on hospital admissions related to a confirmed SARS-CoV-2 infection (per 100,000 inhabitants) as outcome variable for the DID. Due to the small number of hospitalizations in the neighboring border municipalities, this comparison is based on weekly observations from all municipalities of the two neighboring districts (Kufstein and Innsbruck-Land). In Column (4), we found a significant weekly reduction of -7.2 general hospital admissions in Schwaz relative to the municipalities in the neighboring districts. Over the 6 weeks prior to the campaign, the average weekly hospital admissions related to a confirmed SARS-CoV-2 was 11.95. Calculating a semi-elasticity gives a reduction of 39.6% (95%-CI: -54.4 – -20.1). In a similar vein, Column (5) used weekly ICU admissions related to a confirmed SARS-CoV-2 infection (per 100,000 inhabitants) as outcome variable for the DID. We found a significant reduction of 4.1 ICU admissions per week in Schwaz relative to the border municipalities. Over the 6 weeks prior to the campaign, the average ICU admissions related to a confirmed SARS-CoV-2 was 8.89, and the semi-elasticity yields a reduction of 21.3% (95%-CI: -33.3% – -7.1%). However, one should interpret this result with some caution, given that we did not observe a very long time period after the vaccination campaign (hospitalization data ends 7 weeks after dose 2).

Table 1: Two-period DID estimates (before-/after comparison between treatment and control group)

DID-comparison	**New cases** (1)	**VoCs**		**Hospitalization**	
		B.1.1.7 / E484K (2)	B.1.351 (3)	General admissions (4)	ICU (5)
Schwaz vs. border municipalities	-15.56 (-22.5 – -8.6)	-4.43 (-8.0 – -0.9)	-6.05 (-10.7 – -1.4)	-7.18 (-11.2 – -2.6)	-4.14 (-7.3 – -1.0)
Observations	8,085	8,066	8,066	2,489	2,489

Notes: Cases, VoCs and hospitalization in 100,000. DID is based on a before-/after-comparison between border municipalities in Schwaz and the neighboring districts. Daily observations for cases and VoCs, weekly for hospitalization. 95%-CI in in parentheses.

Discussion

This retrospective observational study examined COVID-19 vaccine effectiveness at the population level in the district of Schwaz, an early VoC hotspot that became one of the first highly vaccinated regions in Europe. Our study design is based on several comparisons. We used a control group of districts highly similar to Schwaz regarding many population characteristics, as well as zoomed in on border municipalities residing just outside of the treated district.

We first documented a massive vaccine uptake that raised coverage from around 10% to more than 70% of the adult population within the 5 days of the local mass vaccination campaign in March. Our analysis revealed that this massive rollout of BNT162b2 mRNA vaccine was associated with a significant reduction in new SARS-CoV-2 infections of around 60% relative to the control districts. We find similar, although somewhat lower, significant reductions in

B.1.351 and B.1.1.7/E484K cases. During the time period of our study (up to June 2021), we also observed a small number cases of the B.1.617.2 variant in the control districts but none in Schwaz. Our results suggest that the rapid mass vaccination campaign was successful in curbing the local outbreak of two major VoCs. Our analysis also showed that the drop in cases followed a significant reduction in hospital as well as ICU admissions associated with SARS-CoV-2. Finally, we found the biggest effect of this population-wide vaccine roll-out to occur among younger age cohorts, a mostly unvaccinated demographic group in our control districts (due to the prioritization of older age groups in the national vaccination plan).

A limitation of our study is that it is not a randomized clinical trial but an observational study, which may be influenced by confounders such as lockdown policies. While almost all non-pharmaceutical interventions (such as school measures, or curfew restrictions) were identical for Schwaz and the different control groups, there was an additional SARS-CoV-2 test requirement between the 11th of March and the 8th of April when crossing the border of the district. This test requirement may have affected mobility as well as the spread of infections. However, we analyzed Google mobility data and found, if anything, a slight increase in mobility for Schwaz relative to the synthetic control group (see Supplementary **Figure A2**). Furthermore, we investigated for every other district of Austria with the same test requirement (in total five other districts) if infection numbers dropped in a similar magnitude as they did in Schwaz. None of the five districts experienced a decline in any comparable way after the test requirement (see Supplementary **Figure A3**). Finally, the pattern for the different age groups shown in Figure 3 is difficult to explain by the test requirement policy (which was independent of age). Taking together, our findings suggest that the large reduction of infections in Schwaz was driven by the mass vaccination campaign.

Although previous reports, both clinical trials as well as real-life studies, have shown the effectiveness of the vaccines, studying the overall effect of a vaccination campaign on an entire population is important. Population-wide effects depend on factors which can be controlled for in clinical trials but not in national vaccination plans, such as vaccine uptake of population subgroups, or heterogeneous social mixing. As the district of Schwaz was one of the first regions with population-wide mass vaccination, we believe that our results might be of interest to other global regions. Our results suggest that rapid population-wide mass vaccination can be an effective tool to reduce overall infections as well as to curb local outbreaks of variants of concern. This will be especially important when vaccines become more easily available at a large scale by the end of 2021 (18).

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Data availability

For this study we used data from the Austrian epidemiological reporting system (Österreichisches Epidemiologisches Meldesystem, EMS). These data are collected by the Austrian National Public Health Institute (Gesundheit Österreich GmbH, GÖG), and is provided to the researchers through a restricted-access agreement. Future access to this dataset can be considered through direct application for data access to the GÖG. Sequencing and vaccination data is made available by the Amt der Tiroler Landesregierung, which can be applied for via email.

Code availability

Standard epidemiological analyses were conducted using standard commands in STATA/SE 16.1 (ref. 36). The codes to replicate all the statistical analysis are accessible using the following URL: https://github.com/hwin365/2021_schwaz

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Author contributions

J.P. codesigned the study, performed statistical analyses and cowrote the first draft of the article. H.W. conceived and codesigned the study, performed the statistical analyses and cowrote the first draft of the article. J.K., F.K. and D.V.L. codesigned the study. J.P. and H.W. equally contributed to data collection and acquisition, as well as database development. All authors contributed to the discussion and interpretation of the results, and to the writing of the manuscript. All authors have read and approved the final manuscript.

Competing interest

The Icahn School of Medicine at Mount Sinai has filed patent applications relating to SARS-CoV-2 serological assays and NDV-based SARS-CoV-2 vaccines which list Florian Krammer as co-inventor. Mount Sinai has spun out a company, Kantaro, to market serological tests for SARS-CoV-2. Florian Krammer has consulted for Merck and Pfizer (before 2020), and is currently consulting for Pfizer, Seqirus and Avimex. The Krammer laboratory is also collaborating with Pfizer on animal models of SARS-CoV-2. For all other authors, no conflicts of interests exist. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

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Figures

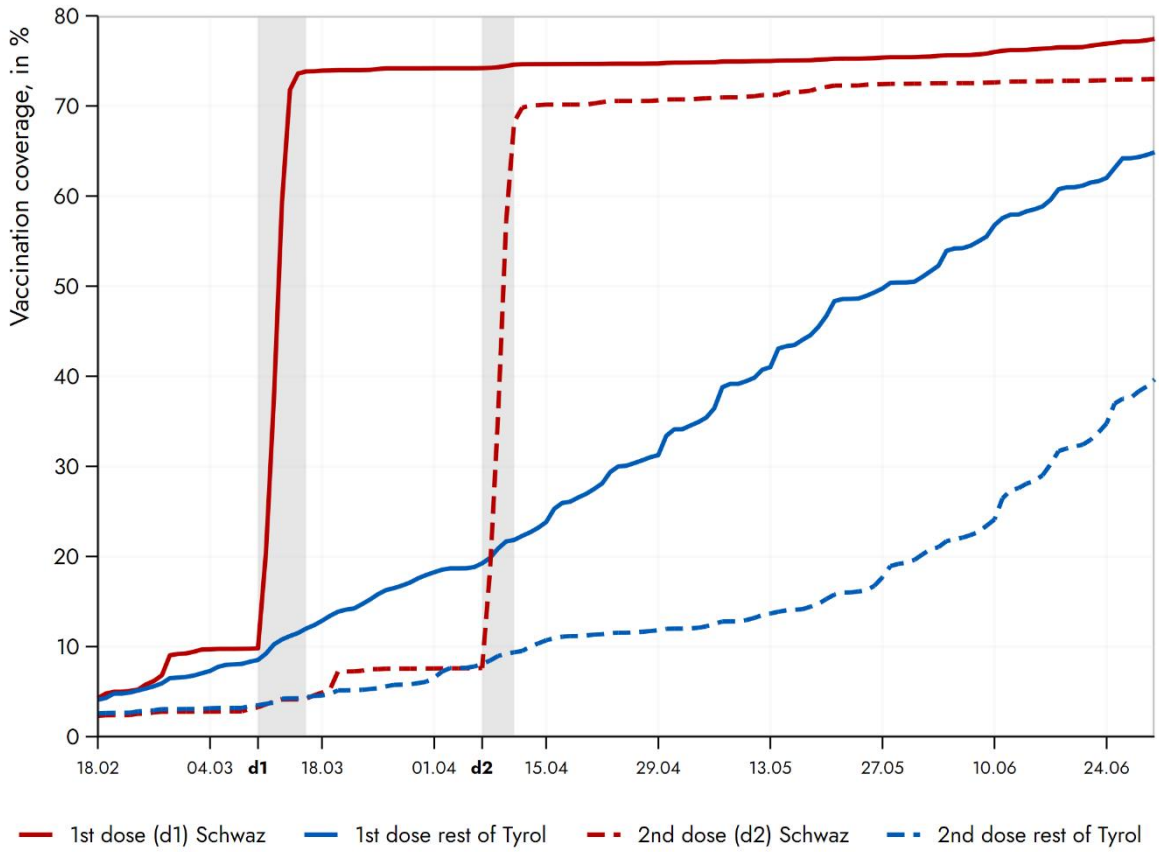

Figure 1. *Vaccination coverage of adult population in Schwaz and the rest of Tyrol*

The figure displays the shares of the adult population that received the first (solid line) and second dose (dashed line), respectively. Schwaz is plotted in red, while the other (eight) Tyrolian districts are pooled and depicted in blue. The shaded areas indicate the period of the first (d1) and the second (d2) roll-out of mass vaccination.

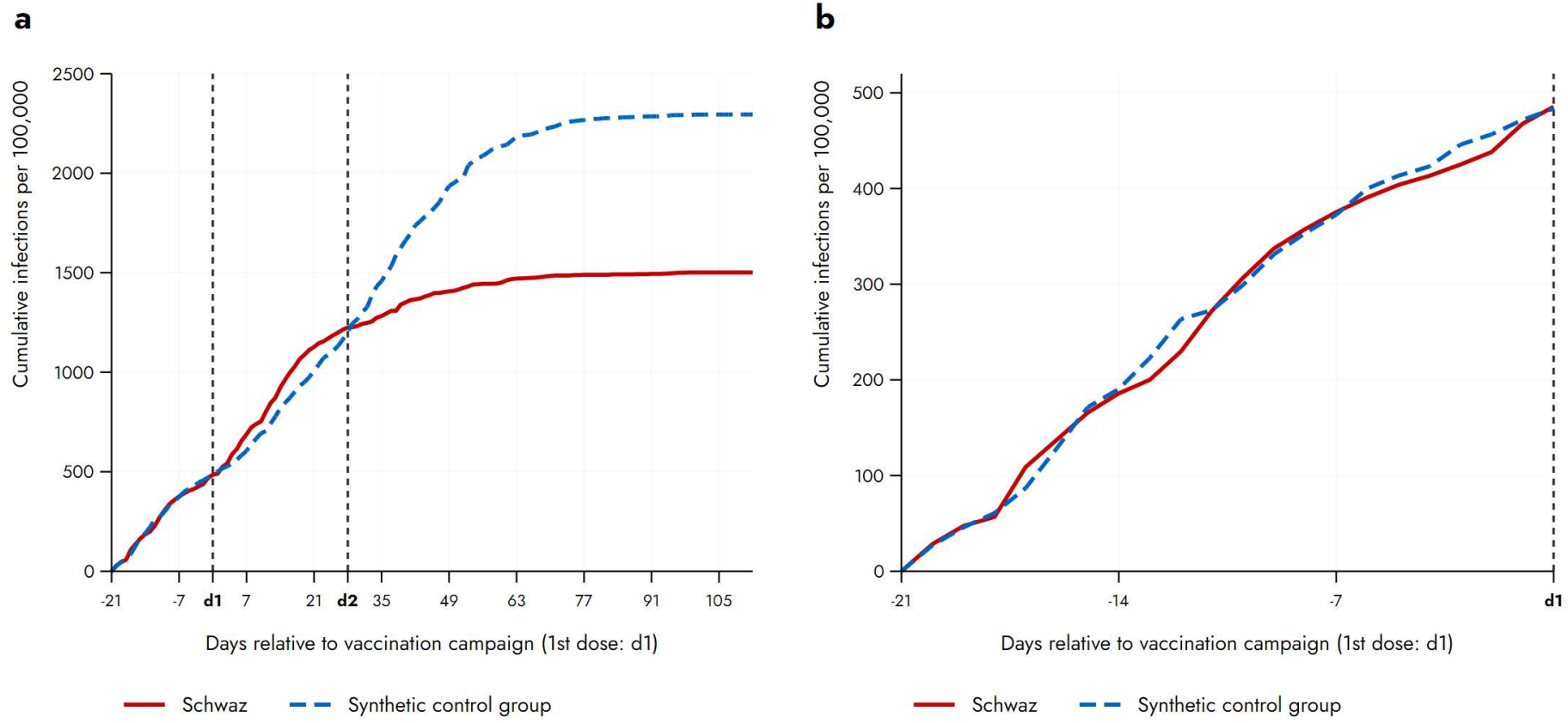

Figure 2. *Cumulative daily infections of Schwaz versus synthetic control group (**a:** after campaign; **b:** before campaign)*

The figure depicts cumulative daily infections (per 100,000) for Schwaz (solid red line) and the synthetic control group (dashed blue line). **a** shows the pre-treatment period, and **b** depicts the post-treatment period. The horizontal axis indicates the number of days relative to vaccination campaign (dose 1, indicated by "d1"). The pre-treatment period started 21 days (three weeks) before the first dose, the post-treatment period ended 112 days (16 weeks) after the first dose. The vertical dashed lines represent the first dose (d1) and the second dose (d2) administered as part of the mass vaccination campaign.

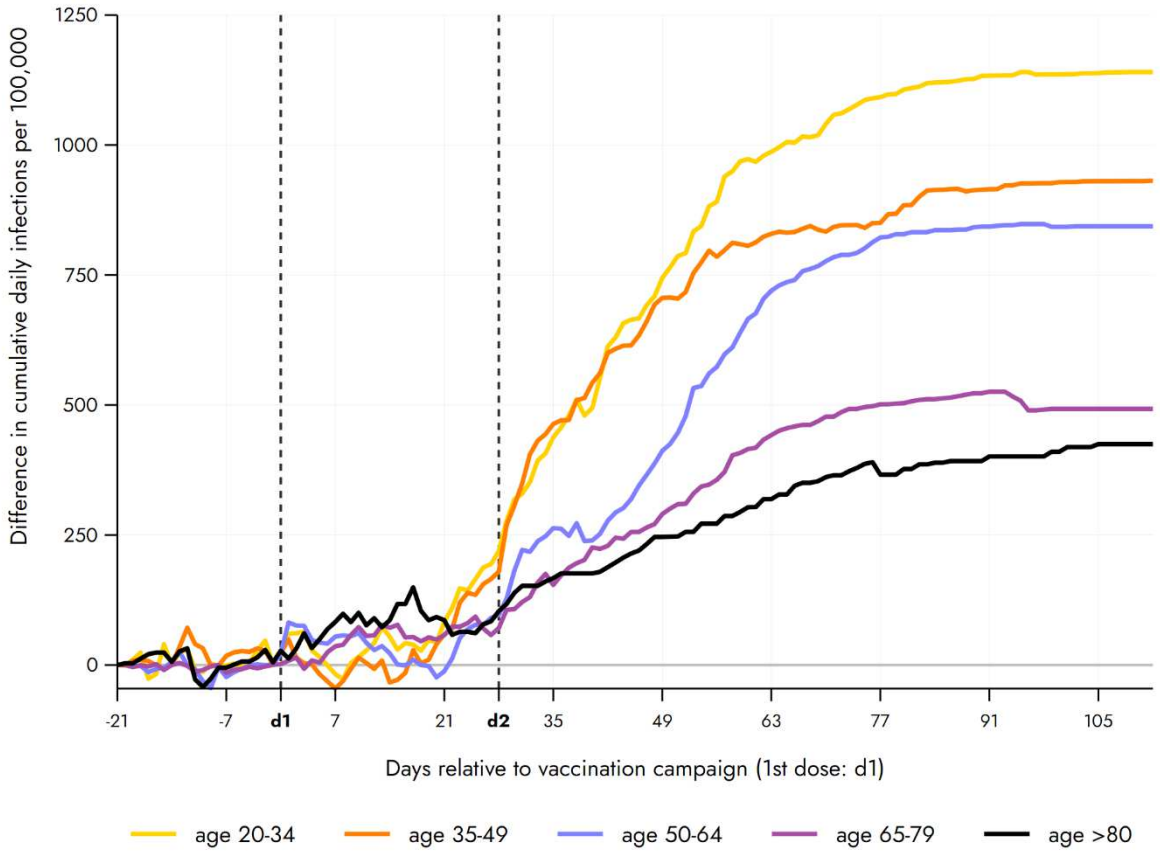

Figure 3. *Difference in cumulative daily infections by age group between synthetic control group and Schwaz*

The figure depicts for each age group in the sample the difference in cumulative daily infections (per 100,000) between the synthetic control group and Schwaz. A positive difference indicates higher infection rates for the control group than for Schwaz. The horizontal axis shows the number of days relative to vaccination campaign (dose 1, indicated by "d1"). The pre-treatment period started 21 days (three weeks) before the first dose, the post-treatment period ended 112 days (16 weeks) after the first dose. The vertical dashed lines represent the first dose (d1) and the second dose (d2) administered as part of the mass vaccination campaign.

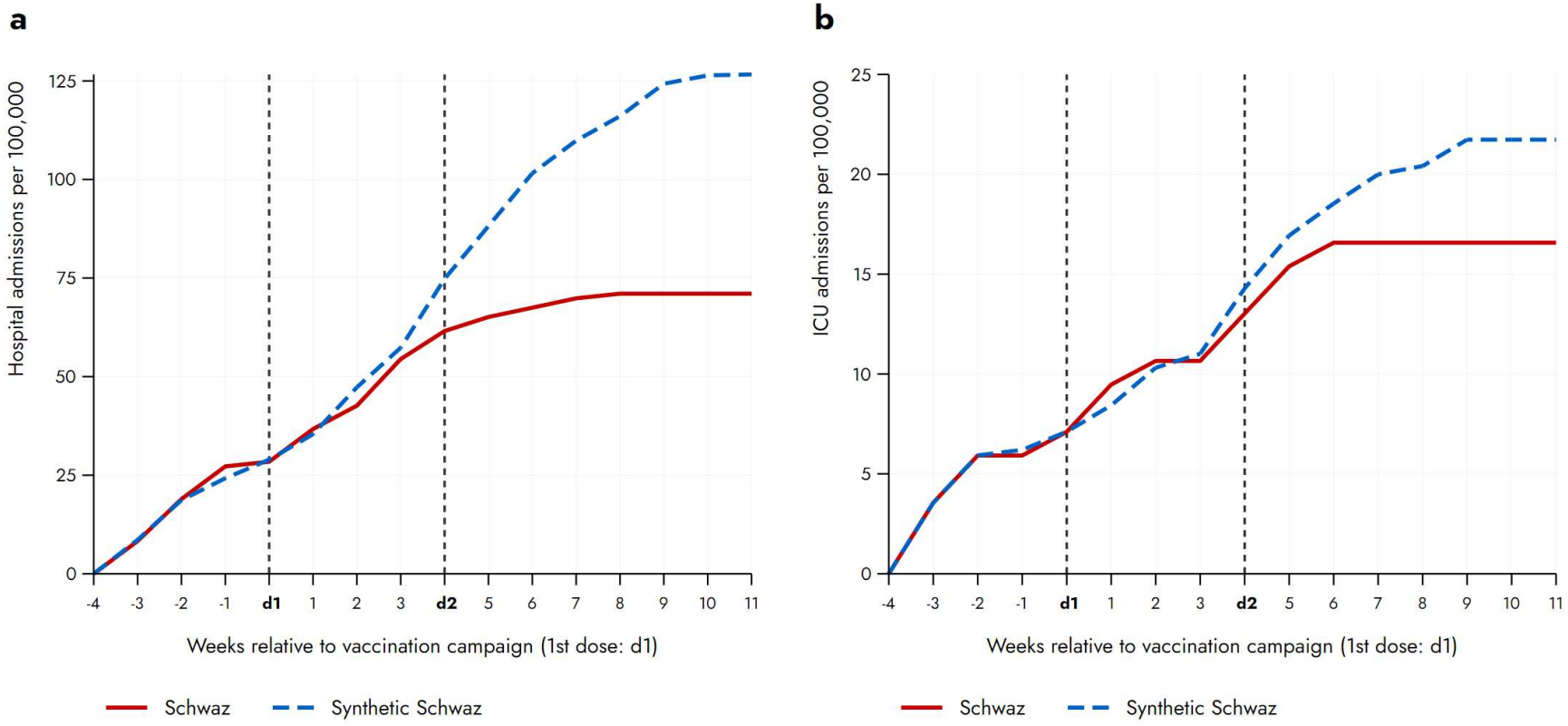

Figure 4. *Hospital* ***(a)*** *and ICU* ***(b)*** *admissions in Schwaz versus synthetic control group*

The figure shows the cumulative weekly hospital admissions (per 100,000) related to a confirmed SARS-CoV-2 infection for Schwaz and the synthetic control group. **a** relates to general hospital admissions, and **b** to the ones in ICUs. The horizontal axis shows the number of weeks relative to vaccination campaign (dose 1). The pre-treatment period started four weeks before the first dose, the post-treatment period ended 11 weeks after the first dose. The vertical dashed lines represent the first dose (d1) and the second dose (d2) administered as part of the mass vaccination campaign.

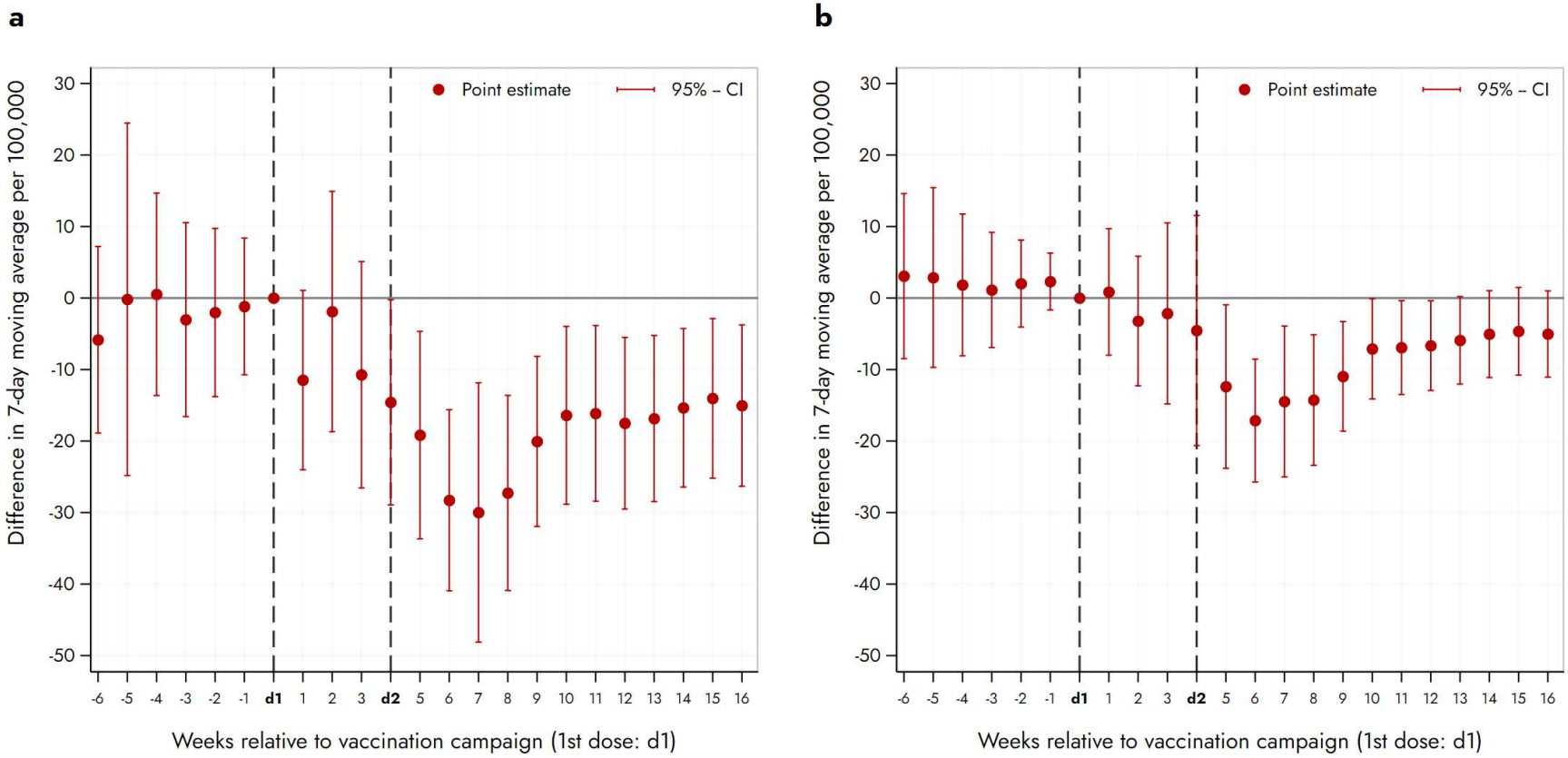

Figure 5. *Daily infections of SARS-CoV-2 (**a:** all infections) and its VoCs (**b:** B.1.351 and B.1.1.7/E484K) in Schwaz and the neighboring municipalities*

The figure displays the results from regression equation (1) and uses the 7-day moving average of daily cases (per 100,000) as outcome variable for Schwaz and its bordering municipalities. **a** refers to all infections, and **b** to the sum of variants B.1.351 and B.1.1.7/E484K. The plotted coefficients represent the weekly difference in the 7-day moving average of new cases between Schwaz and the border municipalities relative to the reference period (week when dose 1 of campaign was administered which is calendar week 10 of 2021). The coefficient for each week is shown together with the 95%-confidence interval. The horizontal axis displays the number of weeks relative to vaccination campaign (dose 1). The vertical dashed lines represent the first dose (d1) and the (d2) second dose administered as part of the mass vaccination campaign.

Supplementary Appendix

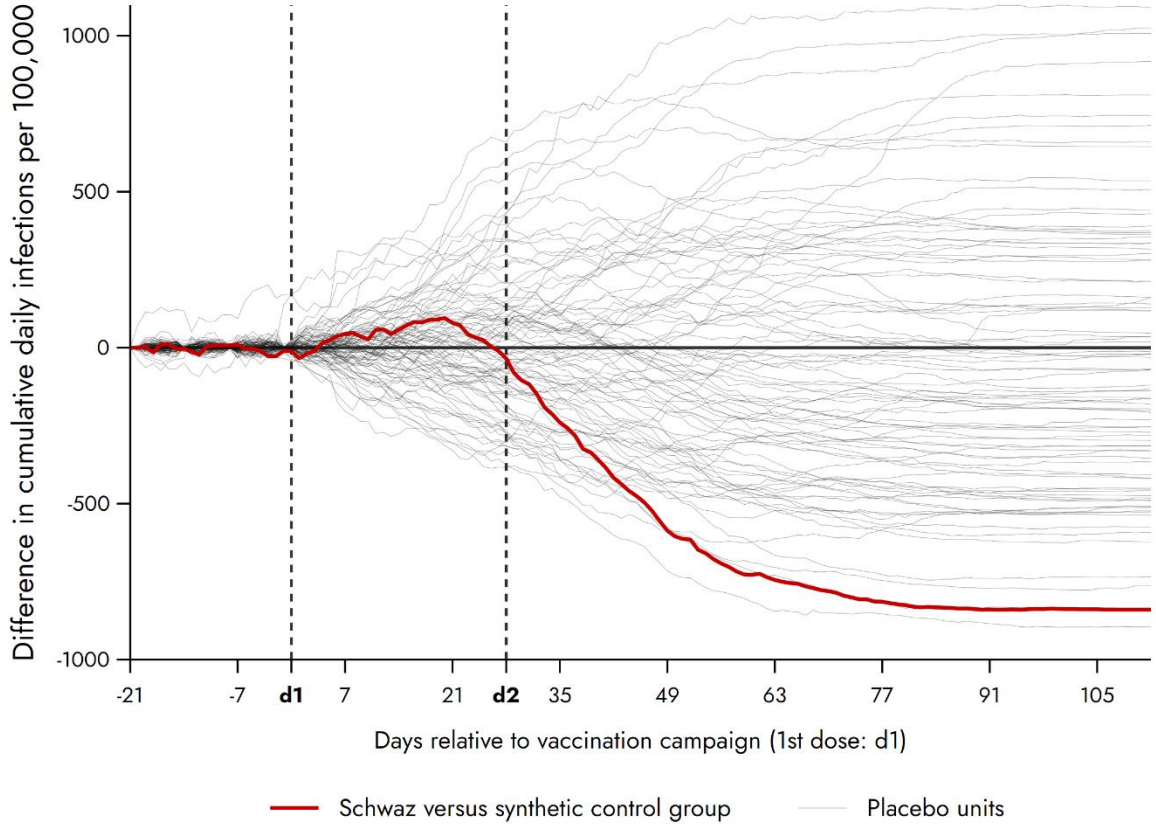

Fig.A1: Placebo-in-space Schwaz versus all donors

Figure A1: *Placebo-in-space Schwaz versus all donors*

The figure describes the results of a placebo test, where we applied the SC method sequentially on each district in the donor pool ("placebo units"), using the date of the roll-out of the first dose in Schwaz as the treatment date (11th of March). It shows the distribution of differences between the treated units and their respective synthetic control units for Schwaz (red line) and each of the 91 placebo units (grey lines) for daily infections per 100,000 as respective outcome variable. Visual inspection shows that the treatment effect in Schwaz was much higher than for almost any other placebo unit. A positive (negative) difference indicates a higher (lower) transmission in the treated group relative to the synthetic control group. Based on the placebo results, we ranked the treatment effects of all 92 districts starting with the highest (negative) effects and performed a standard permutation test. The horizontal axis shows the number of days relative to the vaccination campaign (dose 1, indicated by "d1"). The pre-treatment period started 21 days (three weeks) before the first dose, the post-treatment period ended 112 days (16 weeks) after the first dose. The vertical dashed lines represent the first dose (d1) and the second dose (d2) administered as part of the mass vaccination campaign.

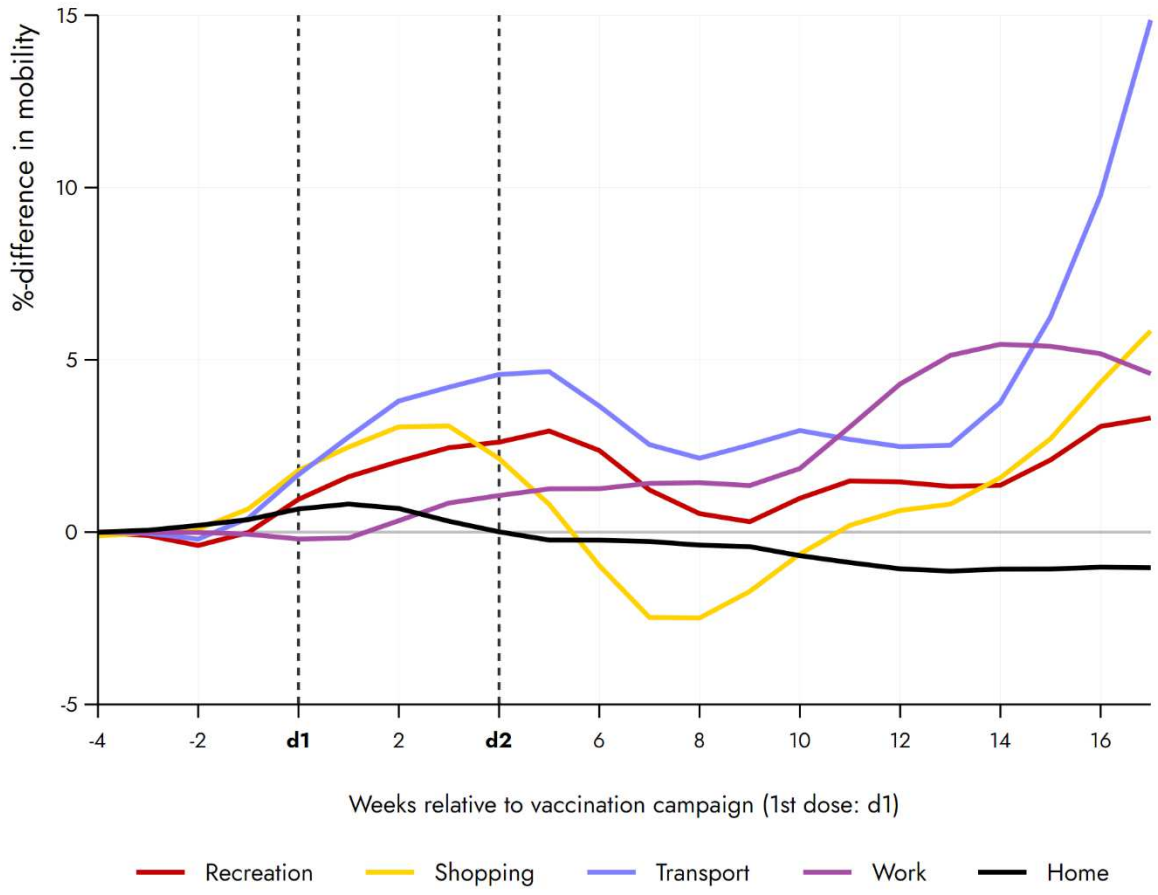

Figure A2. *Mobility patterns in Schwaz versus synthetic control group*

The figure depicts the weekly difference in various mobility measures between Schwaz and the synthetic control group. The mobility measures are based on the Google COVID-19 Community Mobility Reports showing visits and length of stay for five different places and occasions: Recreation (e.g., restaurants, cafes, shopping centers, museums or libraries), shopping (e.g., grocery markets, food warehouses, farmers markets or pharmacies), transport (e.g., public transport hubs such as subway, bus and train stations.), workplaces and residence (home). A positive difference indicates higher mobility in Schwaz than for the control group. The horizontal axis shows the number of weeks relative to the vaccination campaign (dose 1, indicated by "d1"). The pre-treatment period started four weeks before the first dose, the post-treatment period ended 16 weeks after the first dose. The vertical dashed lines represent the first dose (d1) and the second dose (d2) administered as part of the mass vaccination campaign, respectively. *Source*: Google LLC "Google COVID-19 Community Mobility Reports". https://www.google.com/COVID19/mobility/ [July 15, 2021].

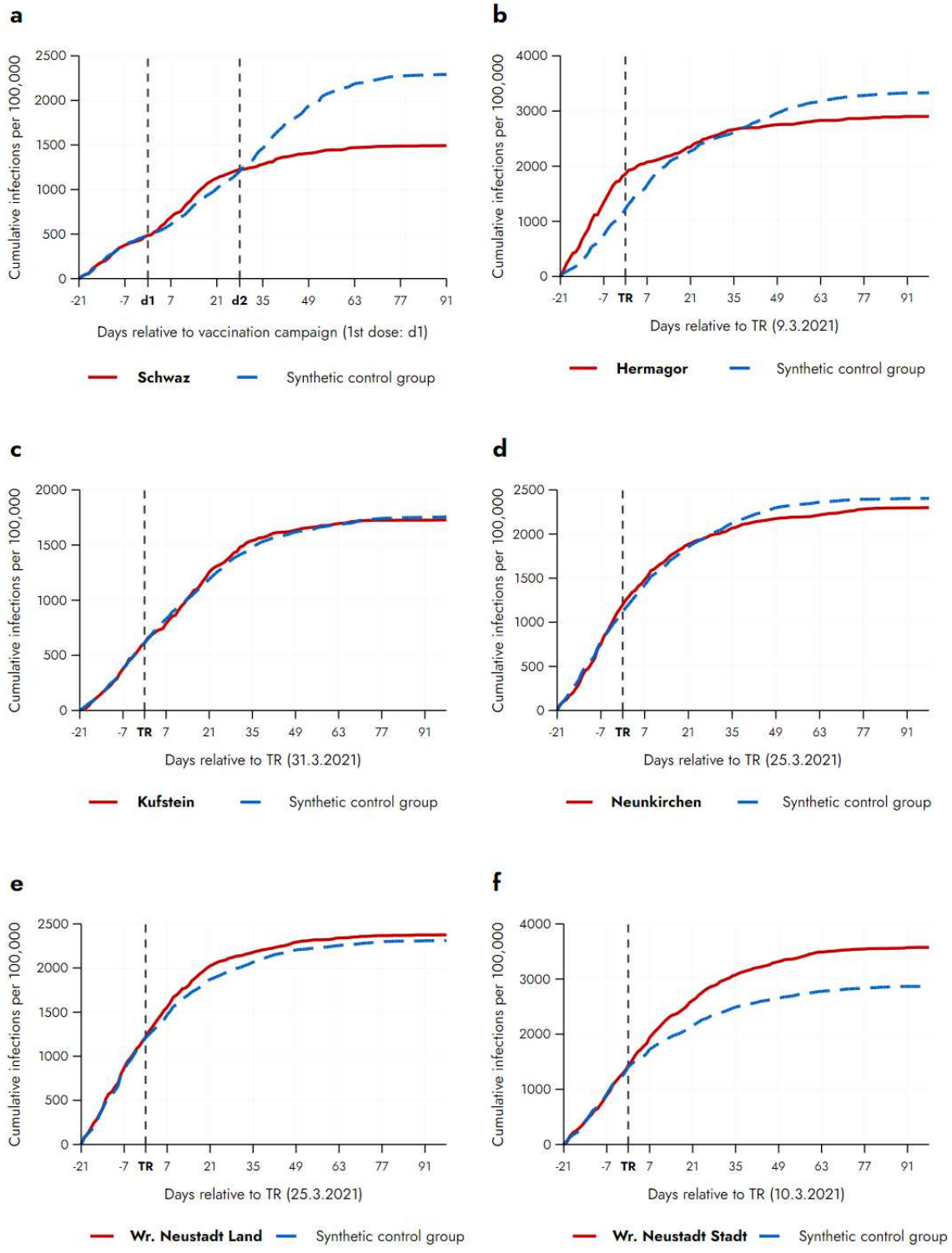

Figure A3. *Cumulative daily infections of Schwaz and NPI-districts versus synthetic control group*

The figure depicts cumulative daily infections (per 100,000) for the five Austrian districts which had a test requirement (TR) in place for crossing district borders and the respective synthetic control group. These five districts are **b:** Hermagor, **c:** Kufstein, **d:** Neunkirchen, **e:** Wiener Neustadt Land, and **f:** Wiener Neustadt Stadt. For comparison, **a** depicts Schwaz versus its synthetic control group, which is identical to **Figure 2** of the main text. The SC algorithm allows a selection of control units that reflect the pre-treatment trend very well. The only exception is Hermagor, where we observe considerable

differences in outcomes between the treatment and the control unit in the pre-treatment period, which in turn makes the post-treatment comparison less reliable. The horizontal axis shows the number of days relative to the respective start of the test requirement (the corresponding starting dates are reported in the legend of the figures), which coincided with the first vaccination campaign week (dose 1) in Schwaz. The pre-treatment period started three weeks before the test requirement, the post-treatment period ended 16 weeks thereafter. The vertical dashed lines represent the first dose (d1) and the second dose (d2) administered as part of the mass vaccination campaign, respectively.

Table A1: *Pre-treatment profiles for Schwaz and the synthetic control group*

Variable	**Schwaz**	**Synthetic Schwaz**[1)]
Infections (day 2)	28.42	27.29
Infections (day 8)	185.90	190.62
Infections (day 14)	357.58	353.56
Infections (day 21)	467.70	472.30
Population	84456	44606.35
Area	1843	1159.37
Number of municipalities within district	39	32.62
RMSPE		12.99

Notes: Infections are measured per 100,000 inhabitants. [1)] Chosen donors include Hartberg-Fürstenfeld (22.8%), Hermagor (11.2%), Reutte (63.8%) and Steyr Stadt (2.2%). The weights for the chosen districts of donor group are reported in parentheses. All other Austrian districts receive zero weight. The RMSPE (Root Mean Squared Prediction Error) measures the difference in infections per 100,000 between Schwaz and the synthetic control group for all pre-treatment periods.