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Supplemental information

Long-term effectiveness of an ultra-rapid rollout vaccination campaign with BNT162b2 on the incidence of SARS-CoV-2 infection

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Supplementary tables

Table S1. Characteristics of REDUCE study participants overall and separately for those who did vs. those who did not participate in the long-term follow-up, related to Table 1.

Characteristic	Overall		Participated in long-term follow-up		Did not participate in long-term follow-up		P-value[a]
	Total no.	Mean ± SD, median (IQR), or %	Total no.	Mean ± SD, median (IQR), or %	Total no.	Mean ± SD, median (IQR), or %	
Age – years	11,955	44.6 (32.2-55.8)	3,859	44.6 (32.3-55.6)	8,096	44.6 (32.1-56.0)	0.419
Female sex	11,955	51.3	3,859	52.5	8,096	50.7	0.061
≥3 persons in household	11,731	54.4	3,802	56.8	7,929	53.2	**<0.001**
Body mass index – kg/m^2	11,893	25.4 ± 4.6	3,840	25.3 ± 4.5	8,053	25.4 ± 4.7	0.421
Smoking status	11,875		3,836		8,039		0.130
Current smoker		26.3		25.7		26.6	
Former smoker		28.6		27.9		28.9	
Never smoker		45.1		46.5		44.5	
Current occupation	11,833		3,830		8,003		**<0.001**
Employed		72.5		73.0		72.2	
Unemployed		12.5		13.4		12.0	
On parental leave		2.6		2.8		2.5	
Retired		12.5		10.8		13.3	
Highest education	11,663		3,772		7,891		**<0.001**
Compulsory school not completed		0.3		0.2		0.4	
Compulsory school		10.4		10.7		10.3	
Apprenticeship diploma		38.3		40.0		37.5	
Vocational school or Advanced level		33.9		35.3		33.2	
University degree		17.1		13.8		18.7	
Prior SARS-CoV-2 infection	11,955	13.8	3,859	13.9	8,096	13.8	0.891
Months since prior infection	1,545	4.0 (3.4-4.6)	503	4.1 (3.4-4.6)	1,042	4.0 (3.4-4.6)	0.591
Other pre-existing conditions							
Cardiovascular disease	11,892	11.4	3,843	11.0	8,049	11.6	0.392
Diabetes mellitus	11,900	2.7	3,845	2.2	8,055	2.9	0.035
Chronic lung disease	11,837	4.2	3,825	3.4	8,012	4.6	**0.002**
Cancer	11,915	3.2	3,849	3.5	8,066	3.1	0.339
Renal disease	11,913	1.2	3,848	1.1	8,065	1.3	0.395
Liver disease	11,898	0.8	3,845	0.6	8,053	0.9	0.116
Intake of immunosuppressants	11,887	1.2	3,839	1.0	8,048	1.4	0.056

[a]P-value for difference between individuals who were versus were not included in the long-term follow-up. P-values are from Mann-Whitney-U-test for continuous non-normally distributed variables, from t-test for continuous normally distributed variables, and from χ^2-test for categorical variables. After correcting for multiple testing, P-values<0.003 (0.05/16 covariates) are deemed statistically significant, which are marked in bold. Abbreviations: IQR, interquartile range; SARS-CoV-2, severe acute respiratory syndrome coronavirus type 2; SD, standard deviation

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Liver disease	11,898	0.8	3,845	0.6	8,053	0.9	0.116
Intake of immunosuppressants	11,887	1.2	3,839	1.0	8,048	1.4	0.056

Table S2. SARS-CoV-2 infections in the REDUCE study during follow-up, related to Figure 1.

	Incident SARS-CoV-2 infections[a]		
	All	**First**	**Second**
Number of events	1,784	1,672	111
Duration of disease – days	9 [6-10]	9 [7-10]	7 [6-11]
Symptomatic			
Yes	1,609 (90.2%)	1,508 (90.2%)	100 (90.1%)
No	158 (8.9%)	150 (9.0%)	8 (7.2%)
Unknown	17 (1.0%)	14 (0.8%)	3 (2.7%)
Respiratory symptoms			
Yes	1,476 (82.7%)	1,400 (83.7%)	75 (67.6%)
No	291 (16.3%)	258 (15.4%)	33 (29.7%)
Disturbance of taste			
Yes	23 (1.3%)	18 (1.1%)	5 (4.5%)
No	1,744 (97.8%)	1,640 (98.1%)	103 (92.8%)
Disturbance of smell			
Yes	22 (1.2%)	18 (1.1%)	4 (3.6%)
No	1,745 (97.8%)	1,640 (98.1%)	104 (93.7%)
Diarrhoea			
Yes	17 (1.0%)	9 (0.5%)	8 (7.2%)
No	1,750 (98.1%)	1,649 (98.6%)	100 (90.1%)
Pneumonia			
Yes	6 (0.3%)	6 (0.4%)	0 (0.0%)
No	1,761 (98.7%)	1,652 (98.8%)	108 (97.3%)
Other			
Yes	339 (19.0%)	275 (16.4%)	63 (56.8%)
No	1,428 (80.0%)	1,383 (82.7%)	45 (40.5%)

Data are represented as median [interquartile range] or number (percentage). [a]One participant had a third SARS-CoV-2 infection and we do not provide more infection-related details in order to protect the participant's anonymity. Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus type 2.

Table S3. STROBE checklist, related to STAR Methods.

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/ rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4-5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6-8
		(*b*) Describe any methods used to examine subgroups and interactions	7-8
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, explain how loss to follow-up was addressed	6
		(*e*) Describe any sensitivity analyses	6-8
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed	8
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9, Table S1
		(b) Indicate number of participants with missing data for each variable of interest	Table S1
		(c) Summarize follow-up time (eg, average and total amount)	9
Outcome data	15*	Report numbers of outcome events or summary measures over time	9, Table S2, Figure 1
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-11
		(b) Report category boundaries when continuous variables were categorized	10-11
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	9-11

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10-11
Discussion			
Key results	18	Summarize key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15-16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-15
Generalizability	21	Discuss the generalizability (external validity) of the study results	15-16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

[a]Period in which BNT162b2 dose 2 (April 8-13, 2021) and dose 3 (November 20-28, 2021) were administered within the REDUCE study.

Supplementary figures

Figure S1. Percentage of individuals vaccinated against COVID-19 with two (Panel A) and three (Panel B) doses in the districts of Tyrol, related to Figure 1.

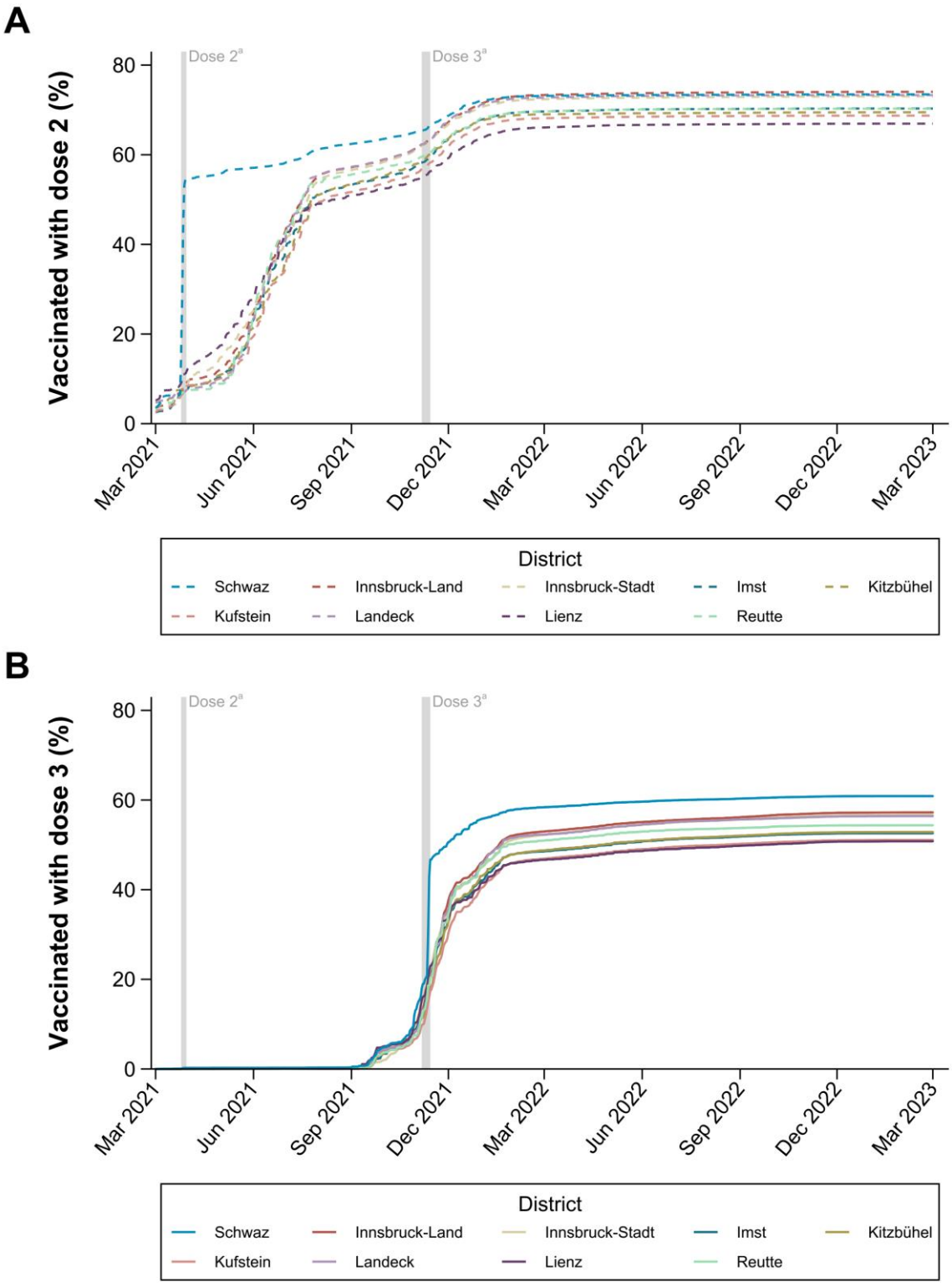
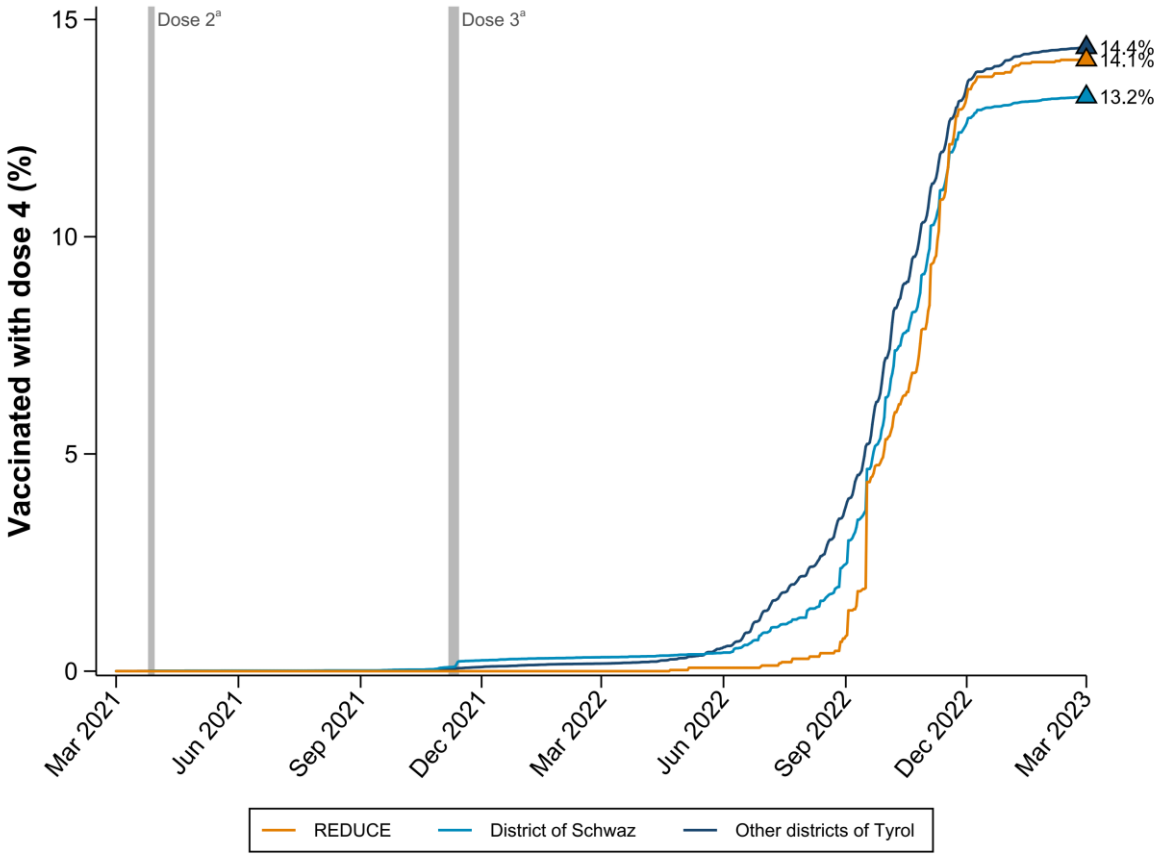
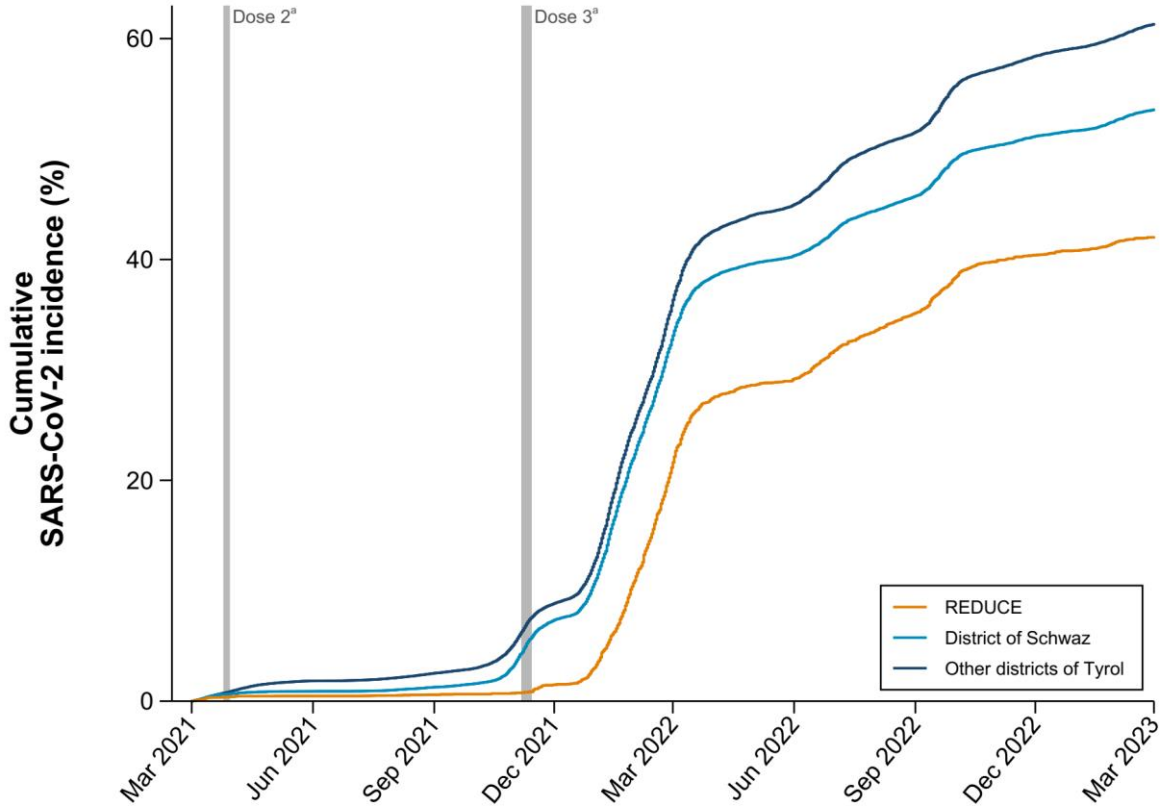


Figure S2. Percentage of individuals vaccinated against COVID-19 with four doses in the REDUCE study, the district of Schwaz, and other districts of Tyrol, related to Figure 1.



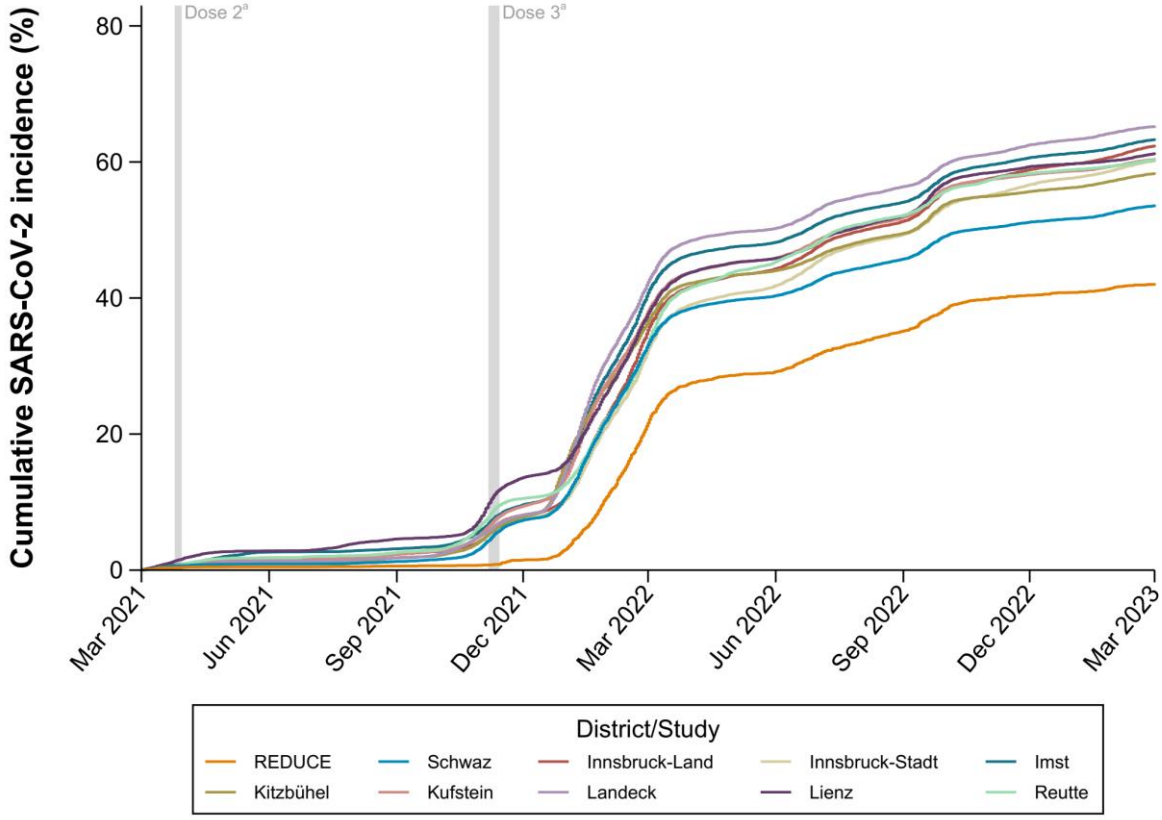
[a]Period in which BNT162b2 dose 2 (April 8-13, 2021) and dose 3 (November 20-28, 2021) were administered within the REDUCE study. Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus type 2.

Figure S3. Cumulative SARS-CoV-2 incidence in the REDUCE study, the district of Schwaz, and other districts of Tyrol, related to Figure 1.



[a]Period in which BNT162b2 dose 2 (April 8-13, 2021) and dose 3 (November 20-28, 2021) were administered within the REDUCE study. Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus type 2.

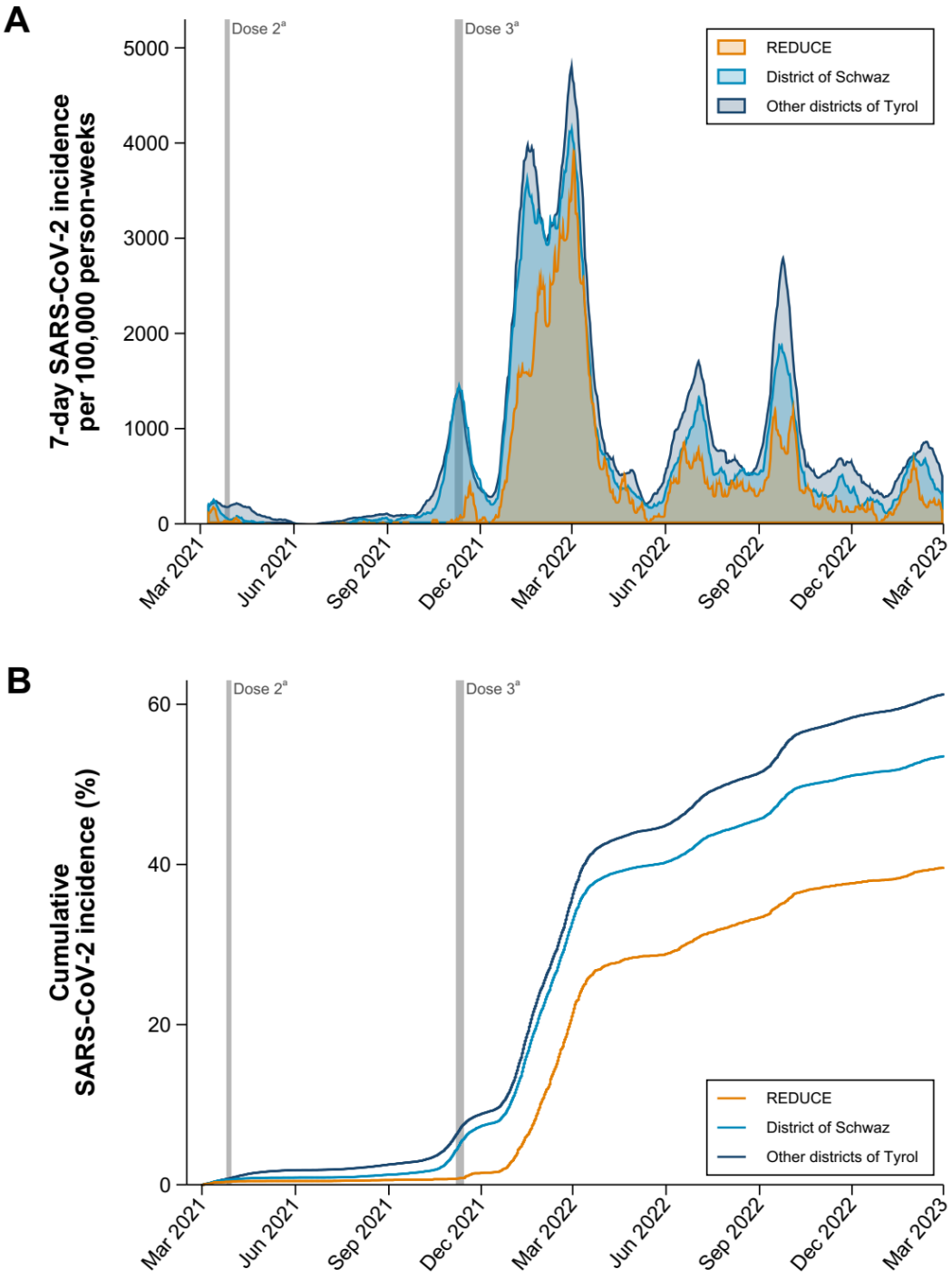
Figure S4. Cumulative SARS-CoV-2 incidence in the REDUCE study and the districts of Tyrol, related to Figure 1.



[a]Period in which BNT162b2 dose 2 (April 8-13, 2021) and dose 3 (November 20-28, 2021) were administered within the REDUCE study. Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus type 2.

Figure S5. SARS-CoV-2 incidence rate and cumulative incidence <u>including recurrent infections</u> in the REDUCE study, the district of Schwaz, and other

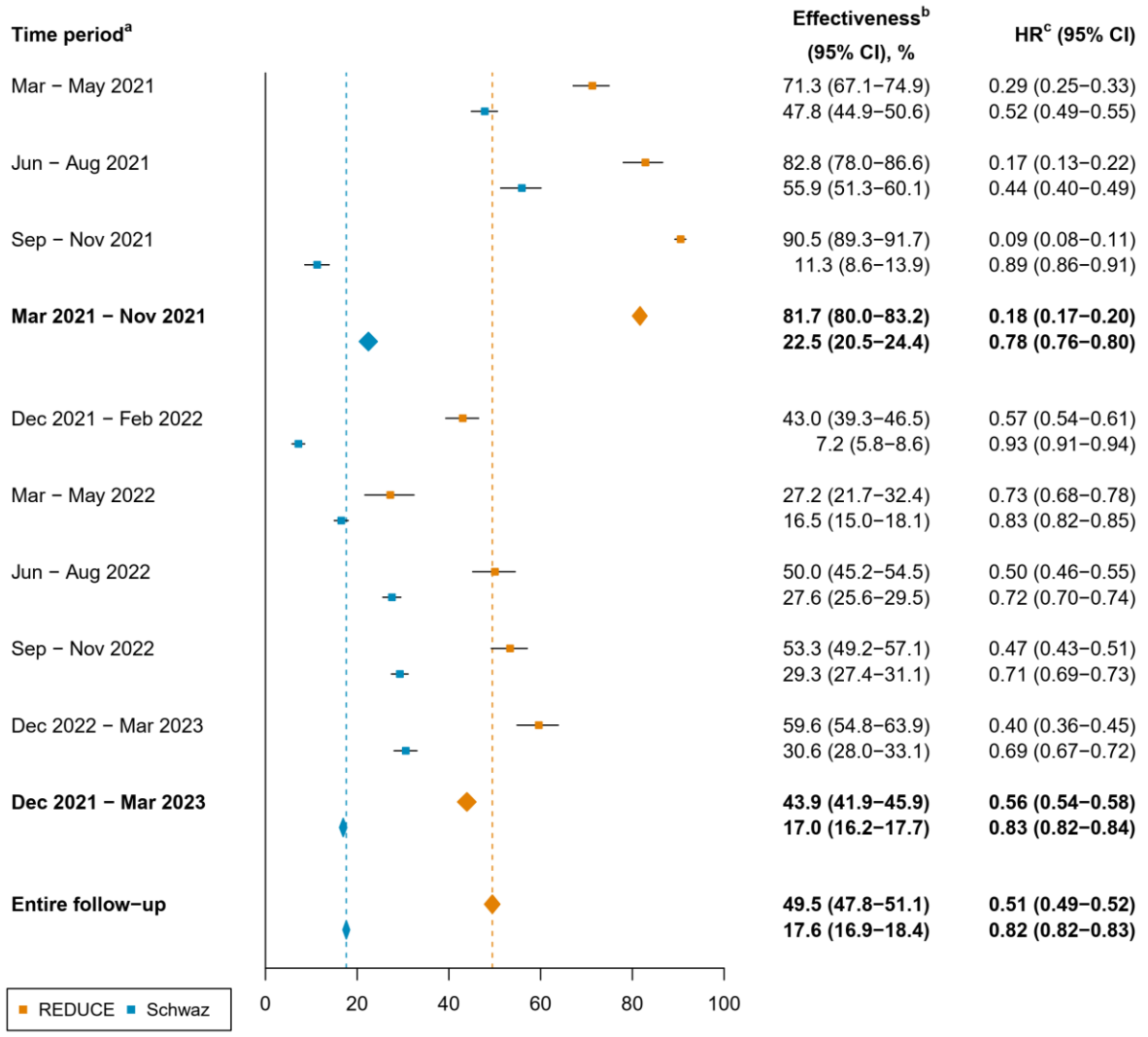
districts of Tyrol, related to Figure 1.



Individuals were considered to be at risk for a recurrent SARS-CoV-2 infection at 91 days after they had experienced an infection. [a]Period in which BNT162b2 dose 2 (April 8-13, 2021) and dose 3 (November 20-28, 2021) were administered within the REDUCE study. Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus type 2.

Figure S6. Effectiveness of the booster vaccination campaign in the REDUCE study and the district of Schwaz compared to other districts of Tyrol <u>including</u>

recurrent infections, related to Figure 2.



Data are represented as effectiveness, defined as one minus the corresponding hazard ratio, and 95% confidence interval. Individuals were considered to be at risk for a recurrent SARS-CoV-2 infection at 91 days after they had experienced an infection. [a]In general, time periods start at the first day of the month first mentioned and last until the last day of the month second mentioned, except for the first period, March – May 2021, which started on March 15, and the last period, December 2022 – March 2023, which ended on March 15. [b]Effectiveness of the vaccination campaign as compared to other districts of Tyrol. [c]Hazard ratio for incident SARS-CoV-2 infection as compared to other districts of Tyrol. Abbreviations: CI, confidence interval; HR, hazard ratio.