

Determinants of SARS-CoV-2 transmission to guide vaccination strategy in an urban area

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Supplementary Material

1 Relevance of Basel-City in a European context - an overview.

Basel-City has to be seen in its larger context: Basel-City is the core city of the trinational Greater Basel area and functional urban area (FUA), according to the official European statistics system. Basel-City is also part of a European cross-border region in the European Employment Services Network (EURES) (FigureS1) that promotes labor mobility across state borders and it

is a main center in the context of “European Regions”. “European regions” are “designer regions” or spaces of cooperation within well defined action perimeters. The role of such forms of regional governance is to foster cross-border cooperation, regional competitiveness with collaborative development plans in interlinked, inter-locking metropolitan regions, which may be organized as “Eurodistricts” and are a mean in the EU-strategy to re-scale and decentralize development through regional institution building. Planning at the Eurodistrict level is regulated by state treaties and can act with a relatively high degree of autonomy from their national governments, mostly in the areas of spatial planning, traffic development and other aspects where links in development are missing.

Moreover, Basel and the Greater Basel area are also part of the Upper Rhine Region Metropolitan Economy, which by regional gross domestic product (GDP) is the eighth largest metropolitan economy in the EU. In summary, the case study of Basel-City is representative or transferable to other similar urban contexts because in the European harmonised statistical classifications (Eurostat and OECD classifications) as a metropolitan area, a functional urban area, and a part of a European cross-border region, it is representative for other urban areas classified similarly. This makes information obtained from analyses of Basel-City comparable and transferable to other such urban areas. This is explained in more detail below.

Basel Metropolitan area: The Greater Basel area is a metropolitan area according the OECD/Eurostat definition, stretching into three countries with a population of around 830,000 in the Trinational Eurodistrict of Basel, an organization of municipalities and cities in the trinational surround-



Figure S1: The EURES-T region Upper Rhine region for the purpose of promoting labor mobility across state borders. These comprise also the four “Eurodistricts” in the Upper Rhine “European region” for the purpose of decentralizing EU structural funds and promoting regional development. The Basel Trinational Eurodistrict is at the bottom.

ings of Basel and central cooperation body in the agglomeration of Basel ¹². Metropolitan regions are NUTS 3 Eurostat statistical subdivisions according to the nomenclature des unités territoriales statistiques - a classification of territorial units for statistical analyses. The NUTS classification provides for a harmonised hierarchy of regions and Eurostat lists 541 such metropolitan areas ³.

Metropolitan areas are engines for growth and employment, the centers of competitiveness, and innovation, and contribute strongly to economic growth, social and political functions and are important for local, regional and international transport. Although only Basel-City, or rather, a small number of city quarters were examined here, Basel-City is a “hub”, i.e. the core of a larger metropolitan region with a commuter catchment area and on a scale that corresponds to the definitions of OECD and Eurostat (European Statistical Office) which also apply to Switzerland. As such, it is the contextualization of the city/urban quarter study within the larger urban/metropolitan/functional urban area, that make the study area comparable with other such metropolitan regions. Using Basel-City as a case study of an urban core or “core city” of its larger urban area / metropolitan area/ functional urban area makes the city, the study area and the results comparable or transferable to other urban areas/metropolitan areas/ functional urban areas and their core cities.

Basel as a hub of a Functional Urban Area: The Greater Basel area is also a functional urban area (FUA) in the official European statistics system. Functional urban areas consist of a densely

¹www.eurodistrictbasel.eu/de/home.html, accessed 18. Feb. 2021

²www.marketing.bs.ch/en/institutional-cooperation/tri-national-cooperation.html, accessed 18. Feb. 2021

³<https://ec.europa.eu/eurostat/web/metropolitan-regions/background>, accessed 18.Feb. 2021

inhabited city and a less densely populated commuting zone whose labor market is highly integrated with the city. FUAs extend beyond formal administrative boundaries. The OECD, in cooperation with the EU, has developed a harmonised definition of functional urban areas (FUAs). Being composed of a city (or core) and its commuting zone, FUAs encompass the economic and functional extent of cities based on daily people's movements Dijkstra et al. (2019). The definition of FUA aims at providing a functional/economic definition of cities and their area of influence, by maximising international comparability and overcoming the limitation of using purely administrative approaches. At the same time, the concept of FUA, unlike other approaches, ensures a minimum link to the government level of the city or metropolitan area. The new harmonized OECD definition of cities, urban areas, functional urban areas and commuting zones allows for the first time a comparison within the European urban hierarchy. It identified 828 (greater) cities with an urban center of at least 50 000 inhabitants in the EU, and the "greater city level" greatly improved international comparability Dijkstra et al. (2019).

Basel-City as part of a European EURES-labor market and labor mobility region: Basel-City is also part of a European cross-border region within the European commission's Strategy of Employment, Social Affairs and Inclusion European Employment Services-EURES cooperation network that promotes labor mobility in the EU and its partner countries in terms of assistance for recruitment and job placements, and providing information to cross order workers and employers on issues such as social security, insurance and taxation ⁴. EURES is based on technical standards and formats required for a uniform system to enable matching of job vacancies with

⁴www.rmtmo.eu/de/metropolregion.html, accessed 18.Feb. 2021

job applications (Commission Implementing Decision (EU) 2017/1257 of 11 July 2017). EU internal border regions cover 40% of EU territory and are home to almost 2 million cross-border commuters. In 2018, more than 1.5 million people in the EU lived in one country and worked in another. In the trinational Basel urban area 60,000 persons commute on a daily basis across state borders, of which around 34,000 commute daily into Basel-City⁵. Just as mobility is an important factor in the economy, it may be a driving factor in the transmission of disease which is why the Basel study may be relevant for other cross-border regions in Europe.

Basel-City as part of a European cross-border region: The trinational Basel metropolitan area with Basel-City as its center has been the first to organize itself in private initiative as a “European cross-border region” in 1960 (Regio Basiliensis e.V.) for the purpose of advancing common interests and developments, enhancing cooperation between regions along state borders and between border regions throughout Europe. It has also served as a model for the institutionalised EU cross-border policy by means of INTERREG funding programs that aimed at promoting decentralized regional development through new forms of governance. Cross-border regions have flourished since the 1990 in particular because of their increasingly relevant role as implementation units for European regional policy in a context of multi-level governance Perkmann (2003). Today, there are some larger 100 cross-border regions as outlined in⁶. Within the nested hierarchy of European “designer regions” for the purpose of fostering regional development some contain the aforementioned Eurodistricts, which are a rather new model of regional

⁵www.statistik.bs.ch/haeufig-gefragt/arbeiten/grenzgaenger.html, accessed 18. Feb. 2021

⁶EURES-T Oberrhein 2021: <https://www.aebr.eu/>, accessed 18. Feb. 2021

governance for promoting economic development in several contiguous metropolitan areas.

Perimeter of Unified Action of European regional governance: The Greater Basel area is furthermore part of the “Trinational Metropolitan Upper Rhine region” (TMUR). This refers to an innovative governance model for the four sub-areas Alsace, France, Northwest Switzerland, Southern Palatinate and Baden, Germany which together form an internationally strong business and knowledge location. The TMUR region refers to a perimeter of unified planning policy measures within a closely interlinked cross-border territory on issues of common interest. As a rather new form of territorial governance the TMUR region acts as umbrella over the existing metropolitan regions and trinational cooperations in the Upper Rhine and aims to strengthen their competitiveness within Europe and the world, and its public positions with respect to the political centers of Berlin, Paris, Bern, and Brussels. Collaborative efforts are focused on the areas of science, the economy, politics and civil society. By regional GDP and population size the TMUR can be seen as a major European metropolitan economy.

Metropolitan areas and metropolitan economies are engines and centers of growth and employment, and their many universities and knowledge institutions are drivers of innovation and international competitiveness. Large urban agglomerations typically combine economic, social and political functions and form important hubs for regional and international connection. Conceptually and methodically it is difficult to view this only in terms of administrative boundaries. The view on large metropolitan areas and regional governance models which encompass multitudes of cities and towns is applied for international comparisons, and in today's

global world the formation of larger metropolitan area governance forms which joins together urbanized areas even across administrative or state borders is the mechanism to achieve joint economic growth. The trinational metropolitan region Upper Rhine, in turn, is a major urban economy within Europe, ranking eighth in terms of regional GDP behind metropolitan areas outlined in Table S1.

Table S1: Selection of European metropolitan areas with GDP, population and GRP. Data obtained from ⁷

	GRP [bio. euros]	Population [mio.]	GRP per inhabitant
Greater London area	946	19.53	48.443
Paris (Ile de France)	709	12.15	58.358
Rhine-Ruhr area	403	9.63	41.850
Randstadt Netherlands	397	8.15	48.659
Milan (Lombardy)	381	10.02	38.023
Brussels-Antwerp	264	5.67	46.656
Barcelona (Catalonia)	224	7.44	30.101
Trinational Upper			
Rhine Metropolitan area	209	5.9	34.889
Frankfurt (Darmstadt)	200	3.95	50.666
Copenhagen-Malmö	180	3.29	54.827
fse Munich	177	6.12	79.690
Berlin	169	3.65	40.104

⁷www.rmtmo.eu/de/metropolregion.html, www.rmtmo.eu/de/wirtschaft.html, www.nl-prov.eu/wp-content/uploads/2017/11/regio-randstad-monitor-2017.pdf, www.nl-prov.eu/wp-content/uploads/2019/05/randstad-monitor-gecomprimeerd-2-gecomprimeerd-compressed.pdf, all accessed 18.Feb. 2021.

2 Reasoning for the study design

Patterns of SARS-CoV-2 transmission have previously been discussed from different angles either via network and transmission modelling Jay et al. (2020), by statistical evaluation De Ridder et al. (2021), or by phylogenetic clustering based on genomic sequencing data Bluhm et al. (2020). Whereas modelling approaches can account for and simulate rich detail such as socioeconomic and demographic information, it is essential to balance the trade-off between detail described and the number of data points available. Moreover, a more diverse socioeconomic and demographic population structure may make it easier to detect general trends. In order to address these needs, many modelling studies rely on publicly available case numbers without being able to relate the cases to specific socioeconomic parameters and specific geographic locations, or have to perform analysis predominantly for large metropolis. For such scenarios, it is inherently difficult to distinguish the spread of competing viral variants within the same population and to account for new introductions in a model - classical ODE or agent-based models are relying on the assumption of uninterrupted transmission chains, information that whole-genome sequencing can provide. Yet given the cost of such analyses, whole genome sequencing covering entire epidemic waves is often infeasible. In this study we address the aforementioned limitations and choose a trade-off between the population detail studies in-light of limited case numbers for which we hold detailed information, including whole genome sequencing: we perform an analysis for a medium-sized, European city to account for the under-representation of these urban areas in previous modelling approaches. The case data used in this analysis was available for 80% of all reported cases in Basel-City and includes detailed, highly sensitive in-

formation on the infected individuals to enable tracing of transmission chains which are not publicly available. Sequencing was attempted for all samples and based on this data we restricted our analysis to inherently related cases of the B.1-C15324T variant. Although reducing the number of cases to <300, this implies that ODE based models are well suited to describe the dynamic development of these cases. We deliberately choose a continuum approach to incorporate socioeconomic, demographic and mobility information into this compartmental model since more complex network approaches would be infeasible for the final number of cases. This model enables us to evaluate general trends of transmission, such as effective reproductive numbers, and to use this information for vaccine scenario building.

In order to complement this more general analysis, we employ phylogenetic analysis to directly trace transmission clusters in detail. Phylogenetic analysis of positive cases provides rich information on relatedness of cases and hence supports modeling approaches by discerning introduction events and community spread. In this study we combine phylogenetic clustering with mathematical modelling of the SARS-CoV-2 transmission pattern. Our analysis is unique in the way that it is based on a large number of sequenced and phylogenetically related cases (411 sequenced out 750 positives, 247 that belong to a single genomic variant). As such, we however hold rich information for a comparably small, yet densely sampled cohort of cases, and are able to provide a complete picture of SARS-CoV-2 transmission in a medium-sized city by choosing two complementary analysis tools.

3 Supplementary Figures

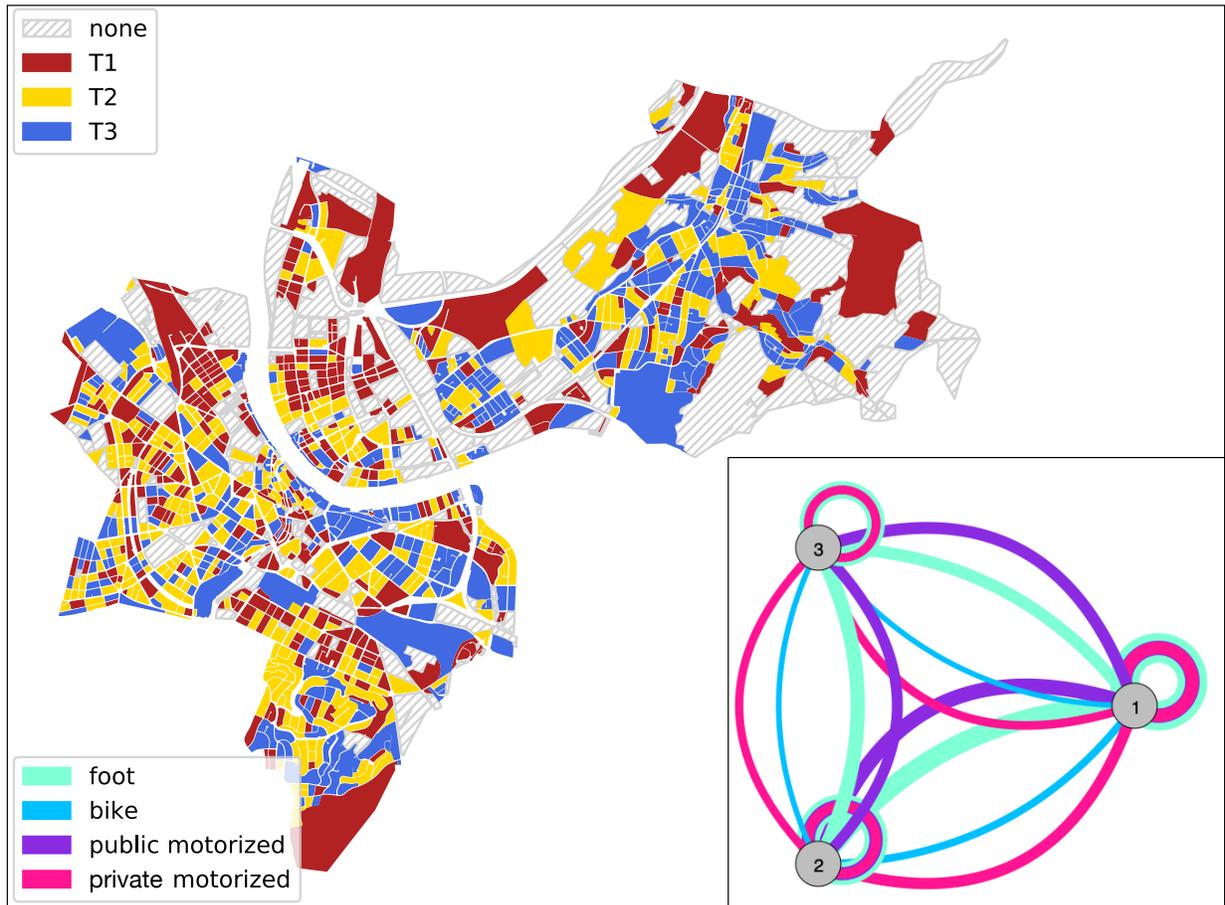


Figure S2: The Canton of Basel-City and its delineation with respect to statistical blocks colored according to the partition into tertiles T1, T2, and T3 of increasing fraction of residents aged older than 64 per block as provided by the canton's office for statistics. Inset: resulting mobility-graph, with nodes representing tertiles and edges representing effective connectedness through mobility by means of various modes of transport (thicker/thinner edges indicating weaker/stronger connectedness), as computed from the traffic-model provided by the traffic department of the Canton of Basel-City.

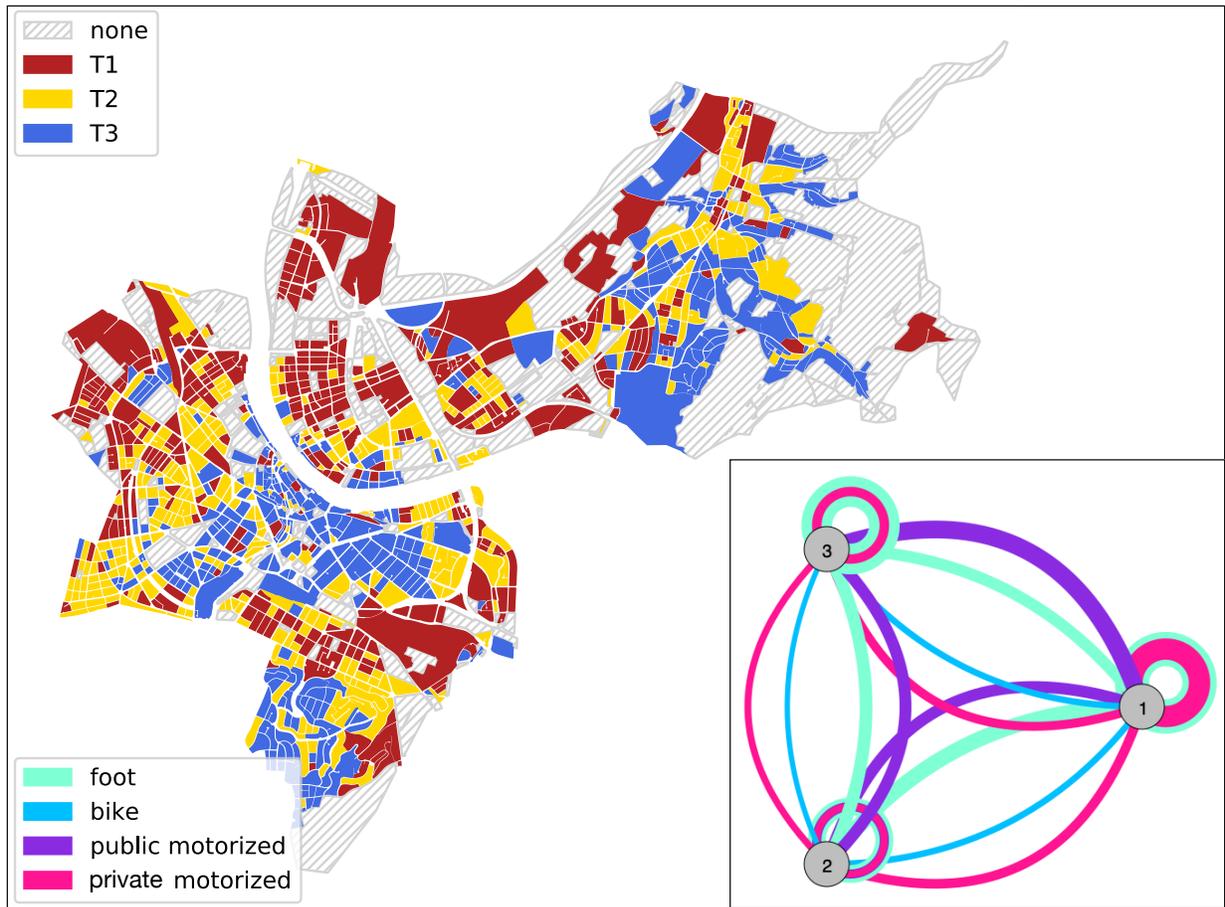


Figure S3: The Canton of Basel-City and its delineation with respect to statistical blocks colored according to the partition into tertiles T1, T2, and T3 of increasing living space per person as provided by the canton's office for statistics. Inset: resulting mobility-graph, with nodes representing tertiles and edges representing effective connectedness through mobility by means of various modes of transport (thicker/thinner edges indicating weaker/stronger connectedness), as computed from the traffic-model provided by the traffic department of the Canton of Basel-City.

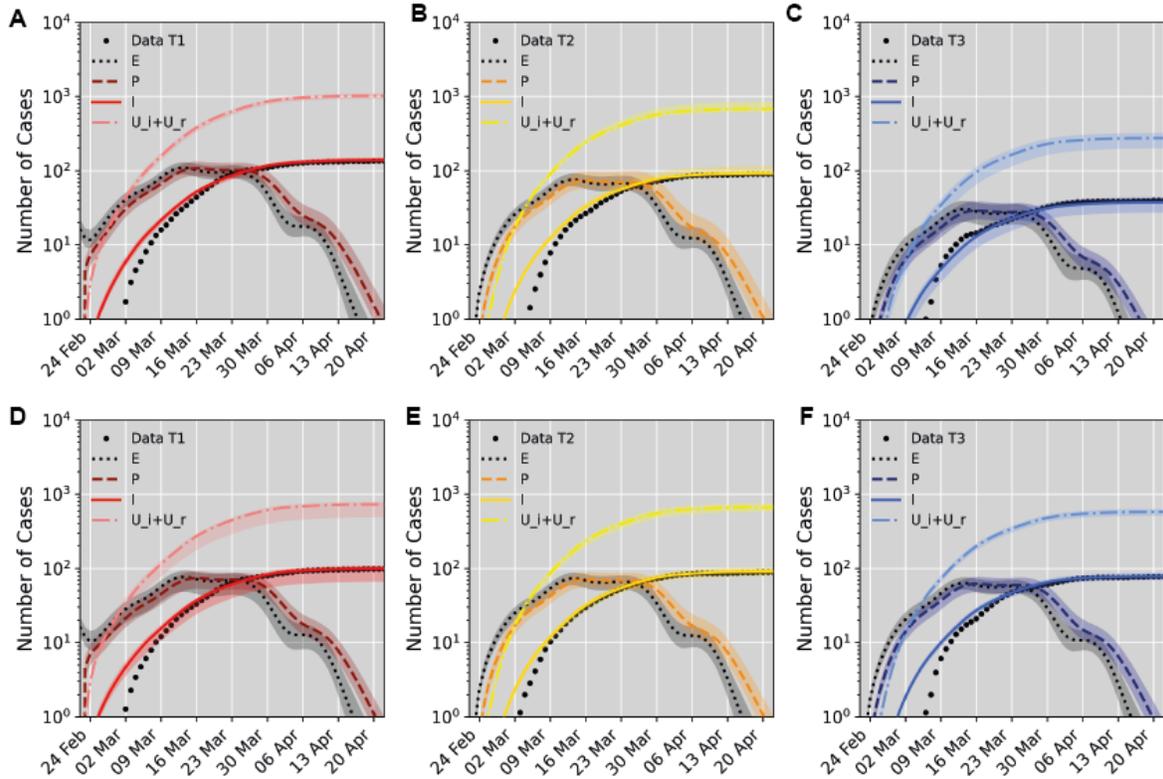


Figure S4: Model fit to data for partitions based on living space per person (A-C) and share of senior residents (D-F). Data points (dots) are shown together with model predictions for compartment I (solid lines, reported infected but isolated cases), the corresponding predictions for compartments E (exposed), P (presymptomatic) and $U_i + U_r$ (the sum of the unreported infectious and recovered individuals) shown as lines with 95% confidence bounds (shaded bands) based on 500 Markov chains. Results are shown individually for each tertile T1(A, D), T2 (B, E) and T3 (C, F). Fits achieved a root mean squared error (RMSE) of 0.98, 0.44, 0.32 cases for absolute and 5.3, 3.2, and 2.5 cases for cumulative cases for T1-T3 for a partition based on living space per person. For a partition based on the share of senior residents: $RMSE_{absolute} = 0.1, 0.24, \text{ and } 0.57$ cases for T1, T2, and T3. $RMSE_{cumulative} = 3.6, 1.6, \text{ and } 2.4$ cases for T1, T2, and T3.



Urban quarters in Basel-City.

Figure S5: Urban quarters in Basel-City.

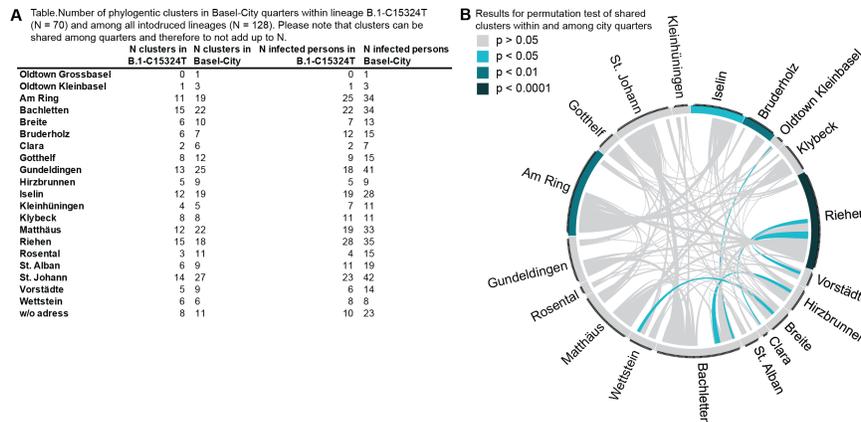


Figure S6: Phylogenetic clusters in quarters of Basel-City. A) Number of clusters within B.1-C15324T and within all viral variants in quarters of Basel-City. B) Visualisation of permutation analysis of shared phylogenetic clusters within and among urban quarters in Basel-City.

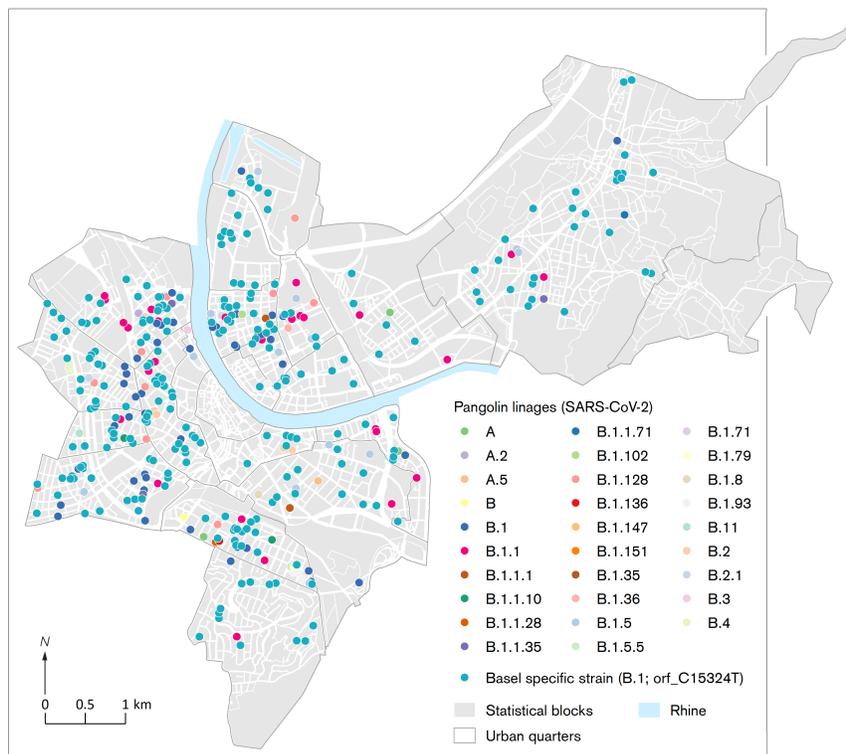


Figure S7: Lineage identity (pangolin) of PCR-confirmed COVID-19 cases from 26th of February until 22nd of April, 2020, in Basel-City with B.1-C15324T as dominant variant highlighted.

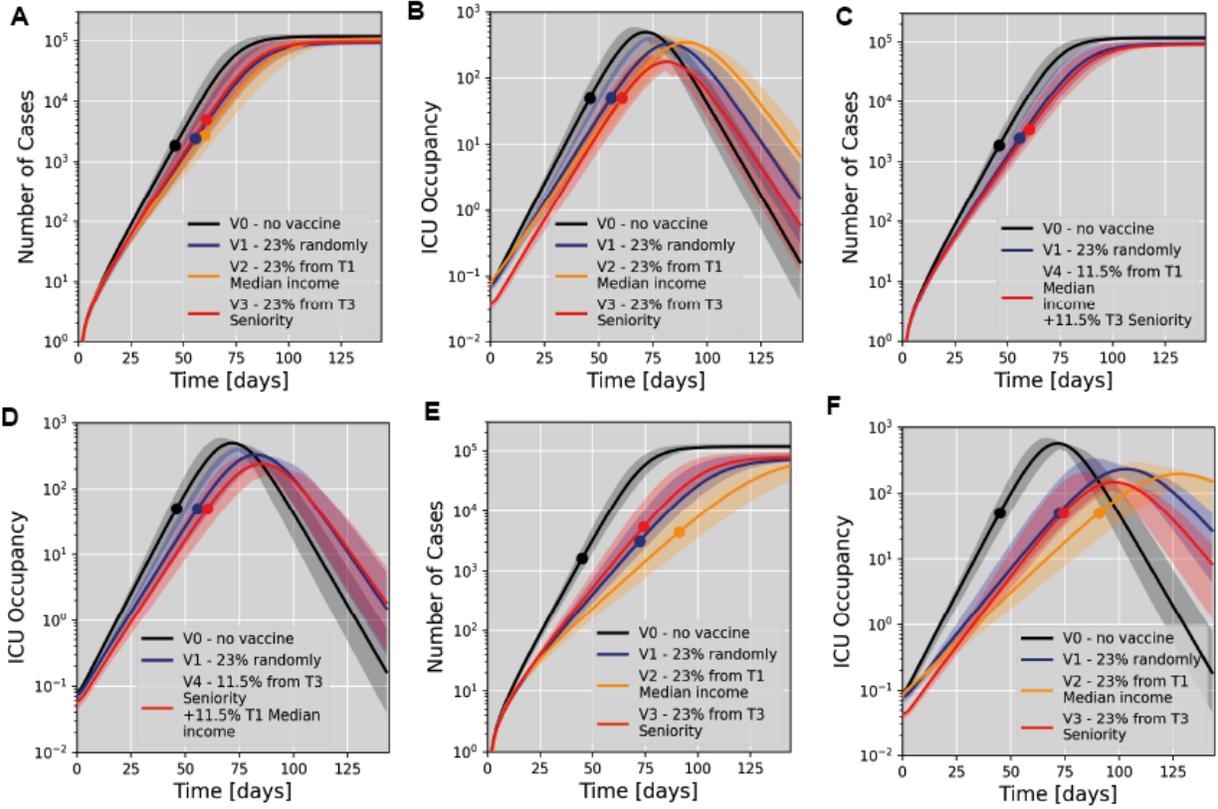


Figure S8: Modelling of vaccine scenarios assuming 60% (A-D) or 90% (E, F) vaccine efficacy to prevent SARS-CoV-2 transmission and 90% (A-D) or 70% (E, F) efficacy against severe COVID-19. We compare with scenarios V0 (no vaccination) and V1 (vaccination at random). Dots indicate the time of reaching a 50% ICU occupancy. A) Simulation of vaccination effects based on a partition according to median income. Scenario V2 models vaccination of 23% of all citizens selected from the tertile with the lowest median income (T1). Scenario V3 models vaccination of 23% of all citizens selected from the tertile with the highest share of senior residents (T3). B) Temporal evolution of ICU occupancy for the scenarios modelled in A). C) Simulation of a mixed vaccination strategy giving equal priority to senior citizens and mobile population groups. D) Temporal evolution of ICU occupancy for the scenarios modelled in C). E) Simulation of the same scenarios as in A) assuming 70% effective vaccination against severe COVID-19, and 90% vaccine efficacy to prevent SARS-CoV-2 transmission. F) Temporal evolution of ICU occupancy for the scenarios modelled in E).

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