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simulation services

Simulation of the SARS-CoV-2 Epidemic in Vienna

Introduction and Aims

The SARS-CoV-2 virus has begun to spread in Austria, too. The attendant Covid-19 cases in Austria are rising at speed and are by now displaying endemic forms. This project aims to model and simulate the spread of SARS-CoV-2, the Covid-19 cases caused thereby and in particular the severe and critical cases that require medical care (hospital stays and/or intensive care units). Scenarios are computed in order to simulate strategies and their effects on the spread of the disease. The aim is on the one hand to locate effective interventions which will reduce the total number of cases, especially the peaks of cases (meaning the maximum value of cases that occur at the same time and require treatment). On the other hand, the required resources need to be estimated and strategies have to be developed in order to safeguard supply.

Scientific Background

The questions described above can only be answered with the aid of an individual agent-based simulation strategy, meaning that each person is considered as one small simulation model (digital twin) within a large model and over the course of time[1]. This is why our Covid-19 simulation model is an agent-based model, which is based on previous work in various projects. Its basis is an agent-based population model (GEPOC[2]) that was created in the context of the Comet K-project DEXHELPP[3] and has since been used as a foundation for a range of simulation questions from the health sector (for example for the assessment of re-hospitalization rates of psychiatric patients[4] and evaluation of MMR and Polio vaccination rates[5]). The model is a stochastic agent-based model and uses state-of-the-art methods in order to guarantee that results can be reproduced, validated and verified (see here, for example[6]).
The epidemic simulation extension to the model is based on an influence simulation model[7] that was developed in a pre-project IFEDH[8]. This model has already yielded new insights into the course of the annual influenza wave in cooperation with the Austrian health system.[9] The contact models are based on data of the POLYMOD study[10] works and contact models developed from the former.[11][12]

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1 F. Miksch, B. Jahn, K. J. Espinosa, J. Chhatwal, U. Siebert, and N. Popper, "Why should we apply ABM for decision analysis for infectious diseases?—An example for dengue interventions," PLoS ONE, vol. 14, no. 8, p. e0221564, Aug. 2019, doi: 10.1371/journal.pone.0221564.

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3 N. Popper, F. Endel, R. Mayer, M. Bicher, and B. Glock, "Planning Future Health: Developing Big Data and System Modelling Pipelines for Health System Research," SNE Simulation Notes Europe, vol. 27, no. 4, pp. 203–208, Dec. 2017, doi: 10.11128/sne.27.tn.10396.

4 G. Zauner, C. Urach, M. Bicher, N. Popper, and F. Endel, "Microscopic modelling of international (re-)hospitalisation effects in the CEPHOS-LINK setting," International Journal of Simulation and Process Modelling, vol. 3, no. 14, pp. 261–279, Jan. 2019, doi: 10.1504/IJSPM.2019.101012.

5 https://www.sozialministerium.at/Themen/Gesundheit/Impfen/Masern---Elimination-und-Durchimpfungsraten/Durchimpfungsraten---Nationaler-Aktionsplan.html
https://www.sozialministerium.at/Themen/Gesundheit/Impfen/Poliomyelitis,-Eradikation-und-Durchimpfungsraten.html

6 J. Ruths, N. Popper, and F. Miksch, "VOMAS for Validation of Agent-based Models – Requirements and Application," in Tagungsband ASIM 2016 23. Symposium Simulationstechnik, Dresden, Germany, 2016, pp. 231–237.

7 F. Miksch, "Mathematische Modelle für neue Erkenntnisse über Epidemien mittels Herdenimmunität und Serotypenverschiebung," Dissertation, Inst. f. Analysis und Scientific Computing, Vienna University of Technology, Vienna, 2012.

8 N. Popper, I. Wilbacher, and F. Breitenecker, "IFEDH - solving health system problems using modelling and simulation," in Proceedings of the International Workshop on Innovative Simulation for Health Care 2012, Vienna, 2012, pp. 127–132.

9 F. Miksch et al., "New Insights on the Spread of Influenza Through Agent Based Modeling," Value in Health - The Journal of the International Society for Pharmacoeconomics and Outcomes Research, vol. 14, no. 7, Nov. 2011.

10 J. Mossong et al., "POLYMOD social contact data," 2017.

11 G. Schneckenreither and N. Popper, "Dynamic multiplex social network models on multiple time scales for simulating contact formation and patterns in epidemic spread," in Proceedings of the 2017 Winter Simulation Conference, Las Vegas, Nevada, 2017, pp. 4324–4335.

12 F. Miksch, G. Zauner, N. Popper, and F. Breitenecker, "Agent-Based Population Models For Household Simulation," in Proceedings of the 7th EUROSIM Congress on Modelling and Simulation, Prague, Czech Republic, 2010, vol. Vol. 2 Full Papers (CD), pp. 567–572.

Methods

An agent-based simulation model for the course of the epidemic in Vienna is expanded and developed on the basis of the GEPOC model[13] that was developed in the Dexhelpp project. This is a population model using statistic representatives for the population of Vienna using the following parameters:

- age
- gender
- place of residence (GPS coordinates, sampled on the basis of registration districts)

Every real person is therefore represented in this model by a virtual image, i.e., a digital twin (called an 'agent' in simulation language). This representative can be followed over the entire timeline. The concept of the digital twin creates absolute freedom to the modeller to evaluate different (prognosis) scenarios in this virtual Vienna. The population is therefore followed, for example, in steps of single days in the basic population model and undergoes processes of death, birth and migration in order to enable a forecast calculation for the population (population status and structure). Find more information on the technical model structure here[1].
The attendant distributions are here taken from data from Statistik Austria[14] and the Global Human Settlement Project[15]. The population model was extended for the Covid19 simulation by providing each digital twin with contact networks which define individual contacts/relationships. Furthermore, the course of the disease is implemented to depict the various stadia of the course of the disease as well as changes to behaviour and the course of treatment due to measures taken.

A city like Vienna has other contact conditions from the rest of Austria: public transport, shopping centres, etc. facilitate many more coincidental contacts and the spatial proximity within a household of two people is less decisive for contact than in rural areas. The model is adapted to these conditions by providing for precisely specified places for human-to-human contacts, such as human-school-human or human-workplace-human networks. Prognoses regarding the spread of the disease are thereby more closely modelled to reality, and it is possible to evaluate scenarios like the closure of schools. Depending on age, gender, income and geographic location of the household they belong to, each virtual person visits different places where contact processes take place per day.

The following location types are currently contained in the model:

- households
- schools (separated into students <14 and >=14 years old)
- workplaces
- leisure time

[13] F. Miksch, G. Zauner, N. Popper, and F. Breitenecker, "Agent-Based Population Models For Household Simulation," in Proceedings of the 7th EUROSIM Congress on Modelling and Simulation, Prague, Czech Republic, 2010, vol. Vol. 2 Full Papers (CD), pp. 567–572.

[14] www.statistik.at

[15] https://ghsl.jrc.ec.europa.eu/

This results in the creation of dynamic contact networks: there are people with whom a person is in contact regularly, such as in the household, at work or other changing contacts with clients or during leisure time. The number and structure of contacts is changed accordingly, when measures are put in place (quarantine measures, closures, changes of behaviour). Parameters include the contact rates from the POLYMOD study (EU project SP22-CT-2004-502084). Very young as well as older people have, for example, clearly fewer contact partners on average than do persons in their twenties and thirties. The same is true for the contact number per day, which also varies by age.
Further locations to be modelled more precisely as next steps are

- childcare institutions
- care institutions for elderly
- large-scale events.

Figure 1: Left: contact network of a single person; Right: contacts (yellow) sampled therefrom for a simulated day

Each contact with an infectious person infected with SARS-CoV-2 by a healthy person is attached to a likelihood of infection (Figure 2). Another decisive factor for the spread of SARS-CoV-2 is, next to contact networks, also the course of the illness as well as the behaviour of the person resulting from that. The model part for the COVID-19 cases therefore gives great significance to the basic patient path, i.e., the series of events that occur in the course of the disease. This requires that disease parameters (sources and assumptions, see appendix 1) are continuously updated with insights and data from published research.
In addition, the measures put in place and the resultant changes of behaviour per person need to be depicted for each point in time. The course of the disease depicted in the model is shown in Figure 3. This includes events that are immediately connected to the course of the disease and that are depicted in a pre-defined order.

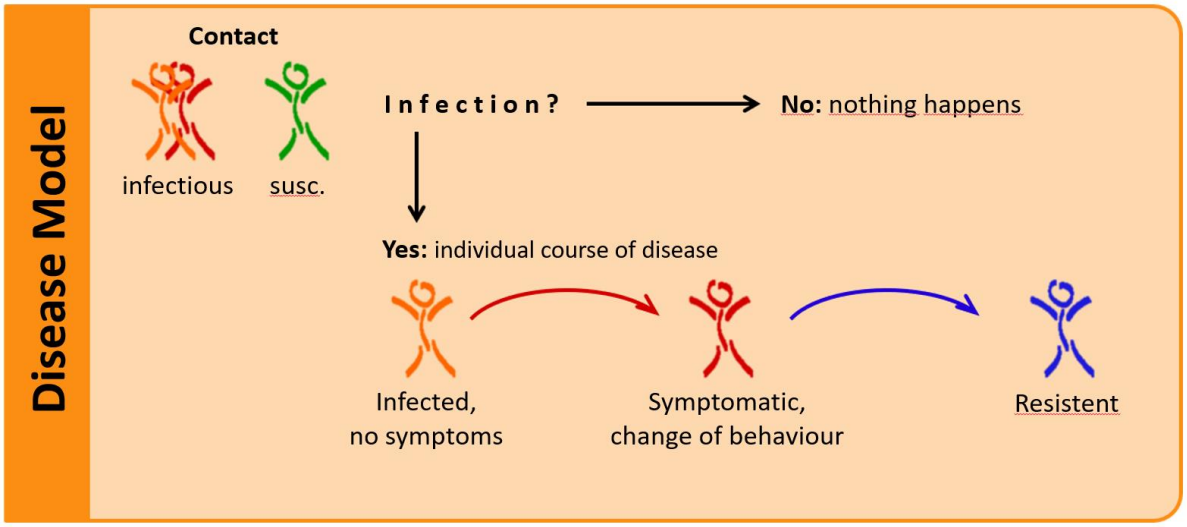

Figure 2: Potentially infectious contact

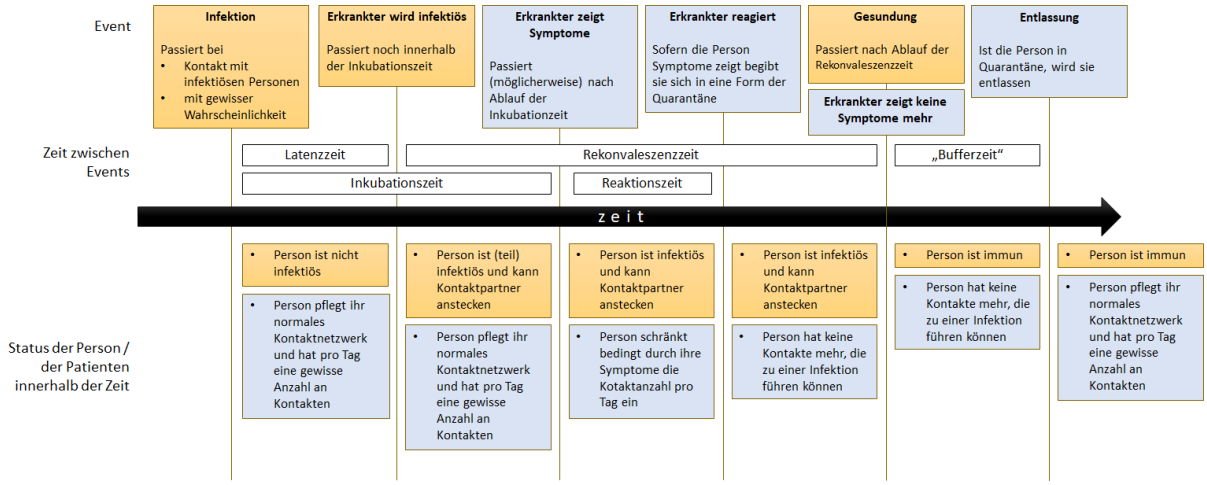

Figure 3: The sequence of events immediately related to the disease currently depicted in the model. Fields with an blue background are actively recognized by the patient or their environment, fields with an orange background are not.

The model also differentiates between 'mild', 'severe' and 'critical' cases in order to be able to evaluate the required resources. The age-dependent distribution of severity is taken from the case number study from China[16] and computed on the Austrian population structure. It is further planned to expand the model with selected chronic diseases in order to be able to simulate particular measures for at-risk patients.

[16] Novel Coronavirus Pneumonia Emergency Response Epidemiology Teamexternal icon. [The Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus Diseases (COVID-19) in China]. Zhonghua Liu Xing Bing Xue Za Zhi. 2020;41(2):145–151. DOI:10.3760/cma.j.issn.0254-6450.2020.02.003.

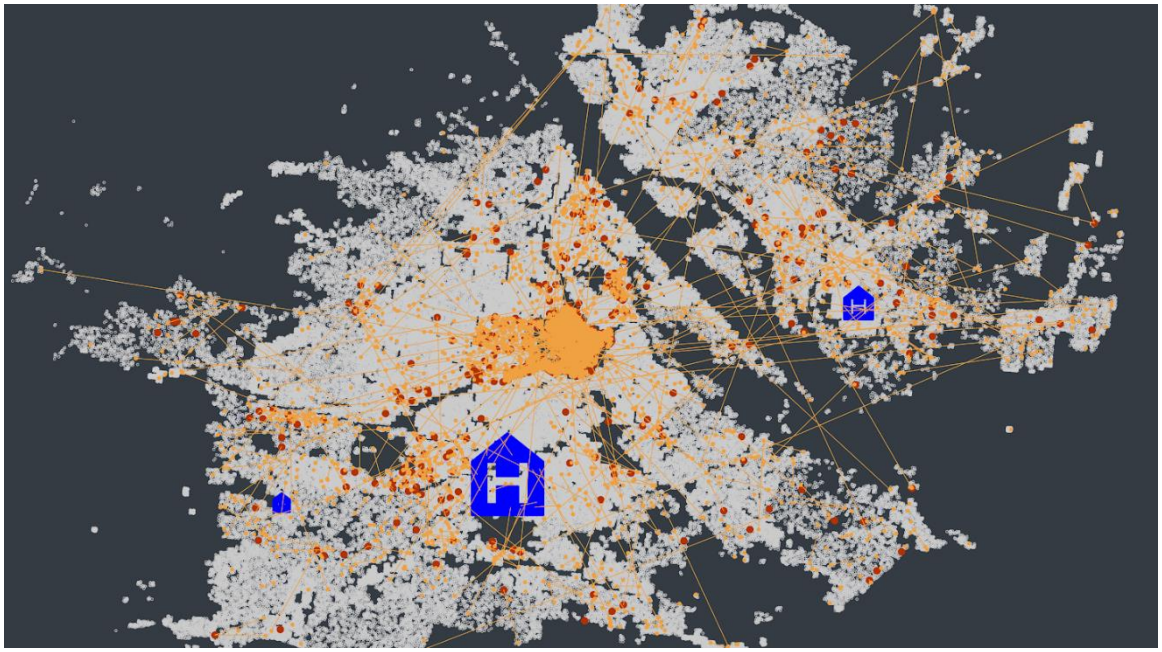

Figure 4: Schematic depiction of the simulation results for a particular point in time in Vienna

A lead time calculation is used in order to be able to depict the startpoint of the simulation as realistically as possible. According to official information, there were fifty confirmed cases in Vienna on 11 March 2020. The simulation starts a model run with a lower number of infected persons (5). These originally infected persons infect further persons in their contact networks. As soon as fifty persons with symptoms are counted in this model run, we stop the lead time calculation. After that, we can adopt all persons infected in the lead time calculations together with the information on the latency and incubation periods that have already passed into the start population for the real simulation.

Scenarios

The individual model versions are used to test different intervention and policy scenarios. As time is of the essence, calculations are continuously being conducted while particular model parts are being expanded in parallel. This widens the range of possible scenarios and increases the quality of the results with each model and data update. The following scenarios are planned:

- Course of the epidemic and confidence intervals if the policies currently in place are maintained
- Calculation of severe cases which require hospital care (resource estimates)
- Cancelling large-scale events
- School closures
- Childcare institution closures
- Increased home office work
- Various quarantine measures

It is an important aim of the calculations to test which measures are able to flatten the epidemic curve so that sufficient resources (beds, etc.) are available and to establish how many are required in the worst case.

The current status of the patient path was already parametrized partly with published data on COVID-19, but is continuously fine-tuned with further expert feedback/input/data. The flexible model structure is able to expand and focus individual areas almost at will, where that serves the precision of the model forecasts. For example, the model is currently fed with non-symptomatic patients, as these have other behavioural patterns than symptomatic patients and therefore have a different effect on the spread of infection. The severity of the disease by age, gender will have to be modelled additionally with other risk factors for the purpose of resource research.

Appendix 1

The following parameters and values are currently (13 March 2020) being used in the model:

Parameter	Application	Value	Sources
Probability of infection	Probability that a contact between an infected and a susceptible person leads to infection	Depends on the contact network in use (~5.8%)	Calibrated to a base reproduction rate R0 of 3.0 (estimate WHO, ARGES)
Incubation period	See figure 1	Beta distribution: 5.1 Median between 2 and 14 days	Lauer SA, Grantz KH, Bi Q, et al. The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application. Ann Intern Med. 2020; [Epub ahead of print 10 March 2020]. doi: https://doi.org/10.7326/M20-0504 // CDC
Latency period	See figure 1	Incubation period minus 1 day	estimate
Symptom – quarantine delay		3.43 day median Weibull distribution (Parameter 4.29; 1.65)	Hellewell, J., Abbott, S., Gimma, A., Bosse, N. I., Jarvis, C. I., Russell, T. W., … van Zandvoort, K. (2020). Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts. The Lancet Global Health. https://doi.org/10.1016/s2214-109x(20)30074-7
Reconva-lescence period	See figure 1	between 7 and 21 days (beta distribution)	World Health Organization (2020). Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19).
Reaction time	See figure 1	Weibull distribution, between 2.02 and 5.23 days, median 3.43	Hellewell, J., Abbott, S., Gimma, A., Bosse, N. I., Jarvis, C. I., Russell, T. W., … van Zandvoort, K. (2020). Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts. The Lancet Global Health. https://doi.org/10.1016/s2214-109x(20)30074-7
'Buffer period'	See figure 1	currently 0 days	
Infectious period		10 days	Woelfel, R., Corman, V. M.,

from onset of symptoms			Guggemos, W., Seilmaier, M., Zange, S., Mueller, M. A., Niemeyer, D., Vollmar, P., Rothe, C., Hoelscher, M., Bleicker, T., Bruenink, S., Schneider, J., Ehmann, R., Zwirglmaier, K., Drosten, C., & Wendtner, C. (2020). Clinical presentation and virological assessment of hospitalized cases of coronavirus disease 2019 in a travel-associated transmission cluster. Cold Spring Harbor Laboratory. https://doi.org/10.1101/2020.03.05.20030502
Households	Household communities	1,2,3,4,5,6+ households each with number of children, adults and pensioners	Statistik Austria (2009)
Unemployed		10.4%	Website Stadt Wien
Schools	School sizes	Truncated normal distribution	Data Statistik Austria 2017
Workplaces	Distribution of the sizes of workplaces		Statistik Austria Workplace survey 2009
Contact partners per day per location	Average number of contacts per day	Each depending on location, gamma distribution	POLYMOD Studie (EU-Projekt SP22-CT-2004-502084) J. Mossong a. o., „Social contacts and mixing patterns relevant to the spread of infectious diseases“, PLoS medicine, Vol. 5, no. 3, 2008. R. A. Hill and R. I. Dunbar, 'Social network size in humans', Human nature, Vol. 14, no. 1, p. 53–72, 2003.
Severe + critical cases	Proportion of cases requiring hospitalization	Age distribution, recalculation of Chinese cases	Novel Coronavirus Pneumonia Emergency Response Epidemiology Teamexternal icon. [The Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus Diseases (COVID-19) in China]. Zhonghua Liu Xing Bing Xue Za Zhi. 2020;41(2):145–151. DOI:10.3760/cma.j.issn.0254-6450.2020.02.003.
Duration of hospitaliza-tion	Period hospitalized cases remain in hospital	Median 10 days (IQR 7.0 – 14.0)	Wang, D., Hu, B., Hu, C., Zhu, F., Liu, X., Zhang, J., … Peng, Z. (2020). Clinical Characteristics of

			138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. JAMA. https://doi.org/10.1001/jama.2020.1585
General death, birth, immigration, emigration rates	Demographic values used in the basic population model	Dependence on age and gender	Statistik Austria
Regional population distribution	Population distribution on the basis of data on Viennese registration districts and informations from the Global Human Settlement map	Dependence on age and gender	Statistik Austria, Global Human Settlement Project
Infected persons at start date (11 March 2020)	Infected persons at start date of simulation	50 known cases with symptoms (list); 140 already infected persons who display no symptoms (by simulation)	Case number list of the Federal Ministry + Calibration