Targeted COVID-19 Vaccination Strategies: An Agent-based Modeling Evaluation Considering Limited Vaccination Capacities (TAV-COVID)

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Executive Summary (Long Abstract)

Introduction

Worldwide, the newly emerged severe acute respiratory syndrome coronavirus type-2 (SARS-CoV-2) and the related coronavirus disease 2019 (COVID-19) led to a significant health, social and economic burden. Severe courses of COVID-19 result in increased mortality and hospitalizations overwhelming many clinical care systems.

Today, more than 100 vaccine candidates including sterilizing and non-sterilizing vaccines are being tested in clinical trials and first market authorization approvals are expected starting end of 2020. The elderly and individuals with comorbidities are at greatest risk for severe courses of COVID-19 and thus would mostly and directly benefit from a vaccination independent on its sterilizing nature. Vaccinating other specific subpopulation (e.g. children, young adults), however, may be optimal to successfully prevent the virus transmission and epidemic spread of SARS-CoV-2 infection as was reported for influenza epidemics. Moreover, vaccinating "system-relevant" groups including healthcare workers would help to maintain healthcare and system services.

As such, systematically investigating the tradeoffs between these strategies is essential to provide evidence-based guidance for health policy decision-making on vaccine distribution, particularly in the initial phases when vaccine availability is limited. Decision makers need to wisely target limited vaccine capacities for subpopulations (e.g., risk groups, healthcare workers, super-spreading hot spots) to optimize overall health and non-health outcomes.

In this study, we used a model-informed approach to quantify the impact of different SARS-CoV-2 vaccination strategies on cumulative mortality and incidence of COVID-19 related hospitalizations as prioritization criteria resulting in different vaccination strategies including strategies with upfront vaccination of healthcare workers in Austria. Our findings may help to inform public health decision makers on the optimal distribution sequence of available SARS-CoV-2 vaccination according to specific benefit criteria, accounting for limited vaccination capacities and adherence to support vaccination prioritization in combination with further containment measures in Austria.

Materials and Methods

In order to assess vaccination strategies that are targeted to specific subgroups and to consider the simultaneous impact on spread, hospitalization and mortality, we applied an agent-based population model, considering the Austrian population represented by about 9 million statistical representatives, taking into account their contact behavior, regionality and COVID-19 specific transmission probabilities and disease parameters.

The project team was advised by members of the Standing Policy and Expert Panel (SPEP TAV-COVID) and other national and international experts on the selection of methods and interpretation of results.

To evaluate the effect of strategies with vaccination of different target groups on multiple outcomes, we considered five upfront defined population groups: (1) elderly: 65 years and older (E); (2) middle age: 45 to 64 years old (M); (3) younger: 15 to 44 years old (Y); (4) vulnerable: individuals with comorbidities leading to severe course of disease (V); and (5) healthcare workers (HC).

Evaluated outcomes of interest were deaths, hospitalizations (intensive care unit (ICU), non-ICU) and new COVID-19 cases avoided. In a first step, we assumed an initially limited number of vaccination doses to vaccinate 200,000 individuals. We have chosen this group size to allow for differentiating even effects on relatively small subgroups during the very first phase of vaccination. In the simulation, the spread of disease in the population is monitored over six months after the vaccination, and the relative risk reductions (RRR) of the outcomes compared to no vaccination were calculated.

In a second step, we performed a sequential optimization analysis to derive a prioritization sequence when in total 2.45 million individuals will be vaccinated. In two independent optimizations, we aimed to minimize deaths and hospitalizations, respectively.

We also simulated scenarios in which the first vaccines were assigned to 200,000 healthcare workers and derived the consequent prioritization sequence for further groups. In addition, we distinguished between scenarios for non-sterilizing and sterilizing vaccines. Sterilizing vaccines provide sterilizing immunity, which is the type of immunity that prevents the virus from establishing an infection. Non-sterilizing vaccines provide effective immunity in preventing (severe) disease but not asymptomatic infection and transmission.

In all simulations, we conservatively assumed an effectiveness of at least 70% in the general population and a reduced effectiveness of 60% for individuals 65 years of age and older. Participation rates in the vaccination program were considered depending on population groups.

Results

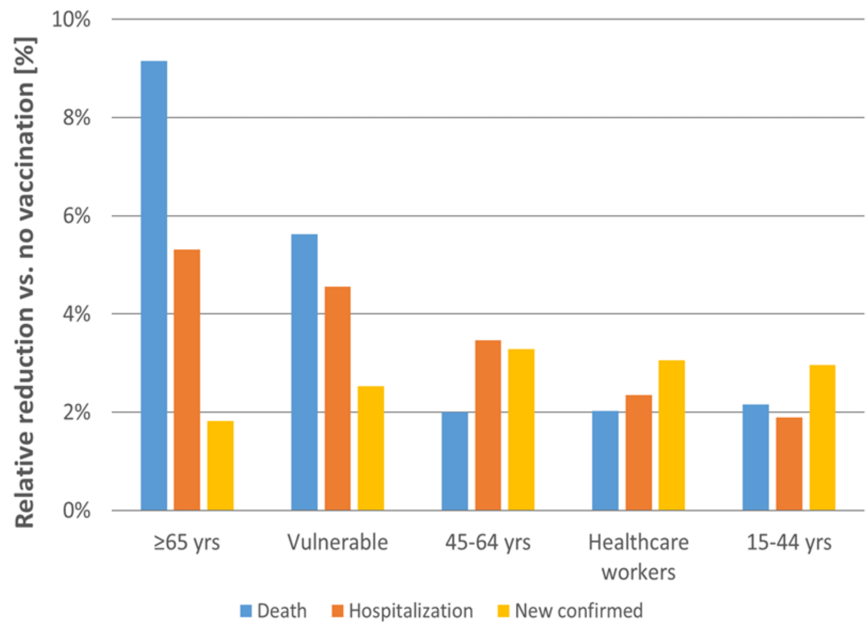
Vaccination of the first 200,000 individuals

The total impact on population level of vaccinating 200,000 individuals in different target groups are displayed in Figure 1 assuming a non-sterilizing vaccine and in Figure 2 assuming a sterilizing vaccine. In both scenarios, the highest relative reduction in deaths and hospitalizations in comparison to no vaccination can be achieved by vaccination of individuals at age 65 or older followed by vulnerable individuals with comorbidities with an increased risk for a severe course of disease once infected.

Figure 1 Total impact of vaccinating 200,000 individuals in different target populations with a non-sterilizing vaccine on deaths, hospitalization and new confirmed infections

yrs – years; Vulnerable: individuals with increased risk of severe disease once infected. Analysis assumed a vaccine effectiveness of 70% in the general population and of 60% in the age group 65+.

Figure 2 Total impact of vaccinating 200,000 individuals in different target populations with a sterilizing vaccine on deaths, hospitalization and new confirmed infections



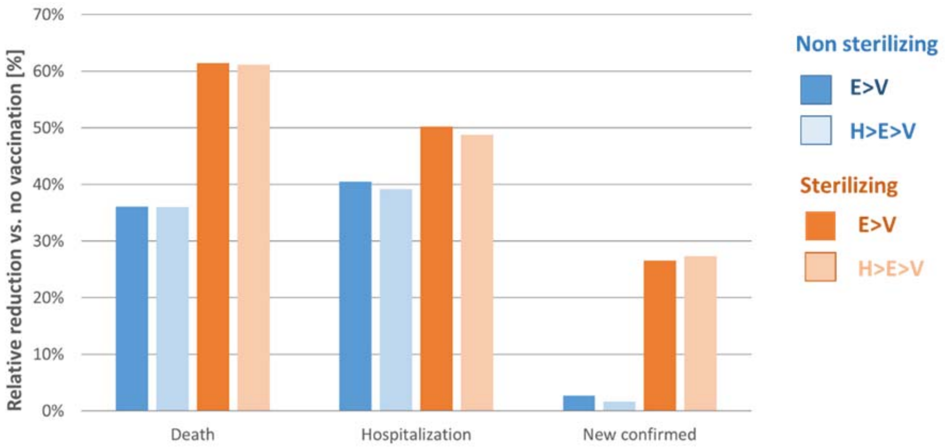
yrs – years; Vulnerable: individuals with increased risk of severe disease once infected. Analysis assumed a vaccine effectiveness of 70% in the general population and of 60% in the age group 65+.

Vaccination of the first 2.45 million individuals

The analysis based on the sequential optimizations for a vaccination of 2.45 million individuals yielded the same sequence, that is, a prioritization of individuals at the age of 65 or older followed by vulnerable individuals. If the first vaccinations are assigned to healthcare workers, the sequential optimizations yielded a subsequent prioritization for individuals at the age of 65 or older, again followed by vulnerable individuals.

Figure 3 displays the impact of these sequential strategies for non-sterilizing and sterilizing vaccines in terms of relative reductions of deaths, hospitalizations, new confirmed cases of COVID-19 infections in comparison to no vaccination.

Figure 3 Total impact of vaccinating 2.45 million individuals as relative reductions in deaths, hospitalizations and new confirmed infections



E>V: starting with the elderly (age 65+), followed by vulnerable individuals with increased risk of severe disease once infected. H>E>V: starting with health care workers, followed by the elderly and then vulnerable individuals. Analysis assumed a vaccine effectiveness of 70% in the general population and of 60% in the age group 65+.

Discussion

If the goal is to minimize COVID-19 related deaths and hospitalizations, elderly and vulnerable persons should be prioritized for vaccination, followed by middle-aged persons, healthcare workers, and younger individuals. However, although prioritizing healthcare workers in the initial phase may result in smaller relative reductions in mortality and hospitalizations compared with prioritizing the elderly or vulnerable persons, additional ethical and system-relevant implications must be considered in this decision. For example, the protection of frontline healthcare workers with a particularly high work-related risk of infection may receive a high priority in order to maximize their occupational safety and to ensure "risk-compensatory" justice in a situation where they are exposed to a higher risk that they cannot escape, in order to serve the society. In addition, following the principle of instrumental and social relevance, the preservation of a functioning healthcare system due to vaccination of health care workers (and other system-relevant groups) must be considered.

Despite all protection measures, healthcare workers may still play a multiplier role in the spread of the disease and a vaccine providing sterilizing immunity to healthcare staff indirectly protects others including residents of nursing homes and vulnerable groups. This aspect follows the principle of utility maximization, but has already been (partially) taken into account in our modeling results, as the model included contacts of health care staff within nursing homes. Finally, logistic aspects and efficiency must be considered in the prioritization decisions. For example, if a mobile vaccination team visits a nursing home to vaccinate its residents, the health care staff of this nursing home should be vaccinated during the same visit to save efforts and avoid loss of vaccine doses in the delivery cold chain.

Assuming availability of a non-sterilizing vaccine for approximately 2.5 million individuals, vaccinating the elderly followed by vulnerable persons avoids approximately one-third of deaths and hospitalizations when compared to no vaccination. In this phase, prioritizing vaccination of healthcare workers yields comparable results. While non-sterilizing and sterilizing vaccines lead to the same prioritization sequences, sterilizing vaccines lead to more effective and sustained reductions in hospitalizations and deaths and, in particular, greater reductions in the spread of infections.

In our simulations, optimization focusing on avoided deaths leads to the same order of prioritization as optimization focusing on avoided hospitalizations. It must be emphasized that these results assume that other protective measures against infectious events are maintained. If the goal is to reduce new infections, different prioritization sequences may result, giving priority to healthcare workers and (younger) people with more work or social contacts. This should be considered in the later phases of the vaccination strategy. We will use our agent-based COVID-19 model with the sequential optimization algorithm and updated model parameters for providing evidence for such phases. Our study has several major limitations. First, the analyses generally do not account for the negative effects of COVID-19-related healthcare worker absenteeism on the outcomes presented. Second, contact behavior and the likelihood of infection of health workers were modeled according to the general population, which may not fully capture the specifics of the work in healthcare. Third, for vulnerable groups, age-specific distributions of risk factors were partially taken from German surveys, which may or may not reflect the Austrian context. Fourth, contact behavior of vulnerable groups was modeled according to the general population. Fifth, we did not consider logistics and time requited for vaccination, that is, we assumed individuals are vaccinated at once at the same time. This simplification has no impact on the results for the prioritization of risk groups. The level of effect of the vaccination may, however, differ when accounting for the timing of vaccination. Sixth, we applied a conservative assumption for vaccination effectiveness of 70% in the general population. Currently approved vaccines showed greater effectiveness in first trials. Consequently, the expected effects of vaccination on defined population level outcomes will be even higher but our sensitivity analyses showed that the prioritization sequence of individuals does not change with effectiveness above 70%. Further vaccines based on various technologies are still in development and effectiveness of these upcoming vaccines is not known yet. It might be, however, that only vaccines with a minimum effectiveness might be approved or used in future.

In the future, the model can be applied to consider further subgroups with respect to social and demographic determinants, timing of vaccination, different effectiveness of vaccine brands or potentially different effectiveness of vaccines caused by COVID-19 mutations and an increased number of available doses of vaccines. We are currently using our model for further analysis in order to provide evidence for policy decisions in later phases of the vaccination program based on updated model parameters.

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The project team was advised by members of the Standing Policy and Expert Panel (SPEP TAV-COVID) and other national and international experts on the selection of methods and interpretation of results. All research results represent the findings generated by the research team and do not necessarily reflect the opinions of the members of the SPEP. The views and opinions expressed during the expert workshops are solely those of the individuals involved and do not necessarily represent the official policy or position of any agency, organization, or employer.

This project is a collaboration of UMIT, dwh and TU Wien.

Conflict of Interest and other Ethics Statements

The authors have no conflict to declare.