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# Кыргызстандагы COVID-19 вакцинациясынын стратегияларын математикалык моделдөө жана анын өлүм

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**Корутунду.** 2020-жылдын аягынан тарта дүйнө жүзү боюнча адамдарды COVID-19га каршы эмдөө иштери башталды. Бирок ресурстары чектелген өлкөлөрдө вакцина жетишсиз болгондуктан, эмдөөнүн натыйжалуу стратегияларын аныктоо үчүн өлкөдөгү COVID-19 боюнча маалыматтар талданган.
Макалада жаш куракка көз каранды SIERS моделин колдонуу менен эмдөөнүн төрт гипотетикалык стратегиясы жана алардын Кыргызстандагы эпидемияга тийгизген таасири салыштырылган.
Ошентип, 2022-жылдын мартына карата коомдук саламаттыкты сактоо системасы COVID-19 учурларын жана аны менен байланышкан өлүмдөрдү азайта алат, эгерде тобокелдиктин жогорку жаштагы топторуна (50 жаш жана андан улуу) көңүл бурулса жана эмдөө орто жаш курактагы адамдарга жазалса (20-49 жаш). Ошондой эле, вакцинацияны дары-дармексиз кийлигишүүлөр менен айкалыштыруунун маанилүүлүгүн белгилей кетүү керек (беткап кийүү жана аралыкты сактоо). Бул COVID-19дан оорунун жана өлүмдүн андан ары төмөндөшүнө алып келет жана башка себептерден болгон өлүмдү кыйыр түрдө азайтат. Ошентип, эгерде бул сценарий байкалса, симуляция мезгилинде (2020-жылдын мартынан 2022-жылдын мартына чейин) өлкөдөгү өлүмдүн көрсөткүчү 27 000ден 16 000ге чейин кыскарышы мүмкүн.
Симуляциянын натыйжаларына ылайык, эмдөө COVID-19дан коргонуунун эффективдүү чарасы болуп саналат, бирок таасири беткап кийүү жана аралыкты сактоо сыяктуу дары-дармексиз кийлигишүүлөрдү эмдөө менен айкалышканда жогорулатат. Тобокелдиктин жогорку топторуна көңүл бурулганда ооруу азаят, андан кийин өлүм. Ошентип, саламаттыкты сактоо системасынын жүгү азаят. Бирок оорулардын жана өлүмдөрдүн кийинки чокусунун азайтуу максатында, эмдөө иштерин жаш курак адамдардын (20-49 жаш) арасында жогорулатуу зарыл.

***Негизги сөздөр:*** *COVID-19, моделдөө, вакцина, Кыргыз Республикасы*

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## Математическое моделирование стратегий вакцинации COVID-19 в Кыргызстане и смертность

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**Резюме.** С конца 2020 года во всем мире началась работа по вакцинации людей от COVID-19. Но в связи с недостаточным объемом вакцин в странах с ограниченными ресурсами, были проанализированы данные по COVID-19 в стране для определения эффективных стратегий вакцинации.
С помощью детерминированной модели SIERS, зависящей от возраста, в статье сравниваются четыре гипотетические стратегии вакцинации, зависящие от возраста, и их влияние на эпидемию в Кыргызстане.
Так, до марта 2022 года, общественное здравоохранение может снизить случаи COVID-19 и обусловленную с ним смертность, в случае повышенного внимания группам высокого риска (50 лет и старше) и умеренной вакцинацией лиц с высокой заболеваемостью (20-49 лет). Также, необходимо отметить о важности сочетания вакцинации с немедикаментозными вмешательствами (ношение масок и дистанцирование), которые приведут к дальнейшему снижению заболеваемости и смертности от COVID-19 и косвенно снизить смертность от других причин тоже. Таким образом, при соблюдении данного сценария, смертность по стране может быть снижена с 27 000 до 16 000 за период моделирования (март 2020 года-март 2022 года).
Согласно результатам моделирования, вакцинация является эффективной мерой защиты от COVID-19, но эффект повышается при сочетании с вакцинацией немедикаментозных вмешательств, таких как ношение масок и дистанцирование. При сосредоточении внимания на группы высокого риска, снижается заболеваемость, далее смертность. И таким образом, снижается нагрузка на систему здравоохранения. Но для достижения эффекта толпы сдерживания очередного пика заболеваемости и смертности, необходимо увеличить охват групп с высокой заболеваемость (20-49 лет).

***Ключевые слова:*** *COVID-19, моделирование, вакцина, Кыргызская Республика.*

## Mathematical modelling of COVID-19 vaccination strategies in Kyrgyzstan and mortality

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**Abstract.** Since the end of 2020, work has begun around the world to vaccinate people against COVID-19. But due to the insufficient supply of vaccines in resource-limited countries, data on COVID-19 in the country were analyzed to determine effective vaccination strategies. Through age-dependant SIERS deterministic model, the paper compares four hypothetical age-dependant vaccination strategies and their impact on the epidemic in Kyrgyzstan.

So, by March 2022, public health can reduce cases of COVID-19 and the resulting mortality, in the case of increased attention to high-risk groups (over 50 years old) and moderate vaccination of people with a high incidence (20-49 years old). It should also be noted the importance of combining vaccination with non-pharmaceutical interventions (wearing masks and distancing), which will lead to a further decrease in morbidity and mortality from COVID-19 and indirectly reduce mortality from other causes too. Thus, if this scenario is observed, the mortality rate in the country can be reduced from 27,000 to 16,000 over the simulation period (March 2020 - March 2022). According to the simulation results, vaccination is an effective measure of protection against COVID-19, but the effect is increased when combined with vaccination of non-pharmaceutical interventions. When focusing on the high-risk group, morbidity decreases, then mortality. And thus, the burden on the health care system is reduced. But to achieve the effect of crowd control of the next peak in morbidity and mortality, it is necessary to increase coverage with high morbidity (20-49 years).

***Key words:*** *COVID-19, vaccination, modelling, Kyrgyz Republic.*

## Introduction

The emergence of COVID-19 vaccines may now change the course of the pandemic. However, it is unlikely that all countries will immediately have sufficient vaccine supply due to a high worldwide demand that will initially exceed manufacturing capacities.

In 2020, GAVI jointly with the World Health Organisation and Coalition for Epidemic Preparedness Innovations (CEPI) initiated COVAX, an international platform, to ensure global equitable access to COVID-19 vaccines and help countries in mitigating the negative impacts on their national health systems and economics. This initiative will enable the countries with limited resources to vaccinate about 20% of their populations by pooling the resources of participating countries and economies (1).

At the time of writing the article, in addition to 226,000 dozes of AstraZeneca provided by COVAX (2) the Kyrgyz Republic received an additional supply of about 1.5 million doses of Sinopharm from China (3) and 80,000 doses of Sputnik-V vaccines from Russian Federation (4). This amount will cover about 30% of the adult population or only 19% of the total population. As of August 9, 2021, about 2.7% of the population in Kyrgyzstan are reported as fully vaccinated and 5,6% as partially vaccinated (5).

This limited amount of vaccines puts the government into a dilemma which groups to prioritize for a better protection of the entire population and lessening of the pressure on the national health system. Currently, the country is going through the third wave of the epidemic with higher incidence compared to the previous periods due to the emergence of the new variants (6). Though the death rates are not that high as in the previous waves, the health system is still overwhelmed with an intensive flow of patients. Thus, during July, almost all COVID-19 attributable hospitals in the capital city Bishkek reported about reaching the capacity threshold of general wards and intensive care unts (7,8).

The existing evidence suggests that disease severity and mortality differ by age (9–12), so that age-dependant vaccination can be considered as an important and priority strategy (13). To date, some countries, mostly with higher incomes and better COVID-19 vaccine coverage, have already shown the effectiveness of vaccination strategies both in regards to morbidity and mortality (5,14–18). Our study adds a Kyrgyz specific perspective to the existing evidence on potential effects of the vaccination on the course of the epidemic in low- and middle-income countries (LMIC) (19–24). Specifically, we modelled four hypothetical age-dependant vaccination strategies to seek for the optimal options in reducing mortality and healthcare demand in Kyrgyzstan. For the practical rational, the national health system's capacity and vaccines availability have been taken into consideration.

## Methods

We applied the web-based interface of the dynamic Susceptible-Exposed-Infectious-Recovered (SEIRS) age-structured model, developed by COVID-19 Modelling (CoMo) Consortium in collaboration with Oxford Modelling for Global Heath (OMGH) Group for the purpose to examine the effect of various intervention packages on the course of the COVID-19 pandemic and related burden on national health systems in more than 150 countries (25,26). The details of the CoMo model framework, equations and parameters can be derived from "COVID-19 Pandemic Modelling in Context: Uniting People and Technology" by R.Aguas and colleagues (27).

## Model parameters

The values of the model parameters describing the disease natural history and clinical course of infection were applied as default for Kyrgyzstan due to unavailability of relevant country specific evidence (25). We applied 16 age groups, defined in the CoMo model, with the probability of contacts within and between age groups based on the social contact matrices for 152 countries by Prem and colleagues (28). For the demographic parameters we used the 2019 United Nationals

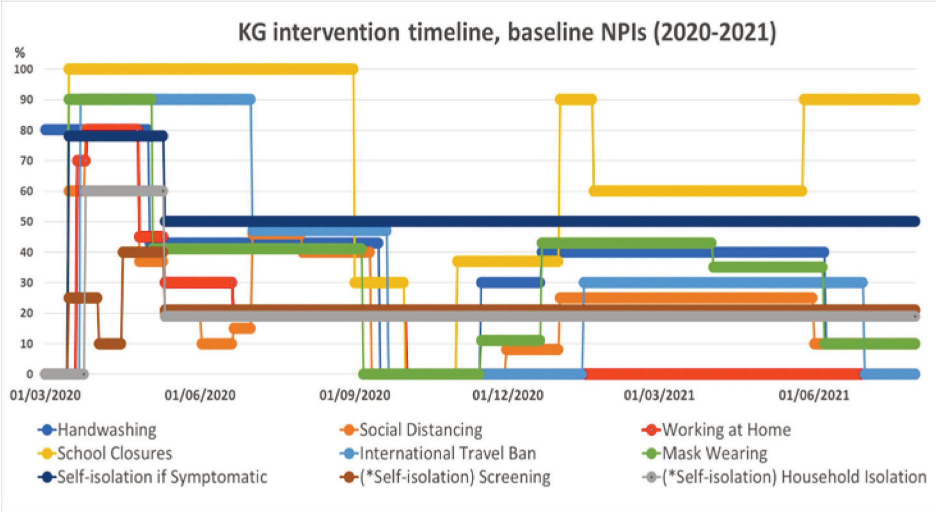


**Figure 1. Timelines of government's chosen NPI strategies and actual behavioural patterns (baseline scenario).**

World Population Prospects Report (29) and data from the Kyrgyz National Statistics Committee (30). The information of the COVID-19 daily new and death cases were derived from the official National COVID-19 online resource (31).

Hospital capacity parameters included the availability of surge and ICU beds and ventilators. We applied internal reports of the Ministry of Health on health system preparedness for the COVID-19 epidemic for the simulation. As for the duration of hospitalised infection for each subcategory (surge, ICU and those under ventilation), we consulted with the Republican Hospital of Infectious Diseases, National Hospital, and the Ministry of Health.

## Baseline interventions

Since at the time of model implementation the vaccination coverage in Kyrgyzstan reached only about 2%, in the baseline scenario we included only non-pharmaceutical interventions (NPIs), which formed a bulk of responses to the COVID-19 epidemic in the country, including self-isolation of symptomatic or laboratory confirmed cases, case tracing, voluntary home quarantining of individuals who contacted with COVID-19 cases, social distancing, hand hygiene, mask wearing, schools closure, working from home, travel ban, and lockdown. The timeline of indicated interventions are shown in the **Figure 1 below.**

We defined the parameter values for Kyrgyzstan based on the estimated population behavioural patterns and prevention measures implemented in the country starting from the epidemic onset up to **June 15, 2021**. Reports and internal documents of the Ministry of Health, Ministry of Education, and Disaster Response Coordination Unit in the Kyrgyz Republic were applied to estimate and define the values for the school closure, travel ban, screening, household quarantining and self-isolation. Due to unavailability of direct parameter values for the social distancing and working from home we applied Google Community mobility report for Kyrgyzstan (32) as a proxy data. The data for mask wearing hand hygiene was based on consultations with local health experts and sociologists.

The model assumes that the isolation of COVID-19 cases and those contacted with them would have lower transmission rate compared to non-isolated cases and their contacts. The changes in social distancing as well as school closure and working from home assume the reduction of social contacts within and between age-groups, while travel ban would reduce the number of imported cases.

## Hypothetical intervention scenarios

Four hypothetical scenarios for vaccination were reviewed in the simulation: 1) Vaccination [65+: 70%, 50-64: 40%, 20-49: 15%] and baseline NPIs ; 2) Vaccination [65+: 70%, 50-64: 40% , 20-49: 15%] and improved NPIs [mask wearing:70% and social distancing:25%]; 3) Improved vaccination [65+: 70%, 50-64: 60% , 20-49: 25%] and baseline NPIs; 4) Improved vaccination [65+: 70%, 50-64: 60% , 20-49: 25%] and improved NPIs [mask wearing:70% and social distancing: 25%]. In these scenarios we measured potential reductions of new reported and unreported cases, deaths, and burden on the health system compared to the baseline scenario. In addition, we estimated how NPIs could improve the effect from the vaccination.

The vaccination coverage is based on the existing evidence on age-related severity and mortality of the disease, planned supply of vaccines in the country (33) and the population structure, which is characterised by a comparatively smaller number of people of older ages

(29). After consulting with local experts we also considered the change of two NPIs in the model, mask wearing and social distancing, as affordable and less disruptive changes in terms of economic and social life of the people. As shown in Figure 1, currently the mask wearing and social distancing are barely followed in Kyrgyzstan.

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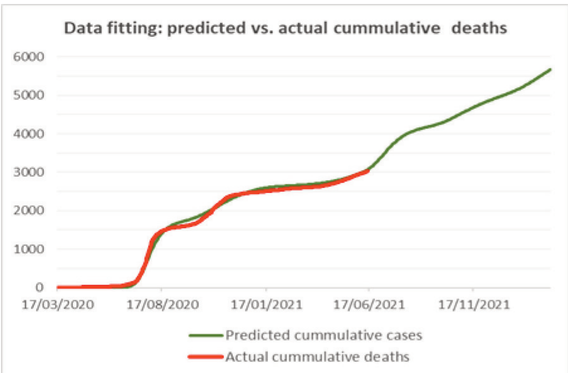
It is important to note that the efficacy of mask wearing, assumed in the model, constitutes 35% only considering the comparatively low level of the availability and affordability of masks in the country and the people's masks wearing behaviour.

## Model validation

Model validation is implemented in two stages: 1) initial visual fitting and 2) particle filtering data fitting (PFDF). The fitting considers the above specified disease and hospitalisation factors, intervention parameters, transmission probability given contacts, proportion of symptomatic and asymptomatic reported cases, hospitalisations reported, and the simulation starting date. The details of PFDF analysis and estimated parameter values are given in **Annex 1.**

Since the reported death cases are assumed to be more reliable compared to confirmed new cases due to low testing capacity and issues with the quality of tests in the country, the fitting is carried out primarily against reported death cases though we applied the fitting against new cases as well. Below are the charts of the predicted data calibrated against actual reported cumulative death cases and daily new cases **(Figure 2 A and B):**

**A)**




**B)**

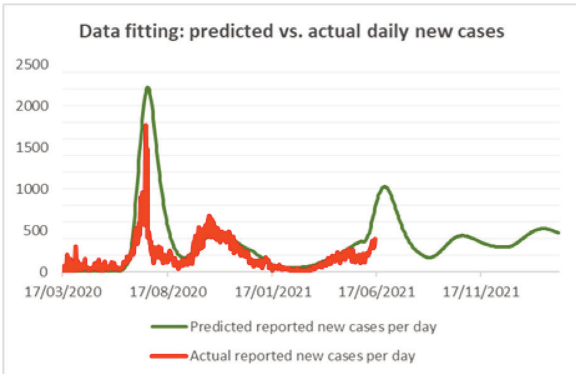



**Figure 2. Particle filtering data fitting of the projected epidemic curve against actual reported cumulative death cases (A) and daily new cases (B) as of June 15, 2021.**

## Limitations

One of the major limitations is that the model accounted for the preliminary COVID-19 variant only, since at the time of the modelling the option of projecting the scenarios with new variants was not available in the web based application. Accordingly, the actual effect on the epidemic and related health outcomes from the vaccination may have different outcomes from the prediction depending on which variant(s) will prevail in the country.

The other limitation is that due to the limited available information for the Kyrgyz context we used some key parameter values based on the assumptions and estimations for the simulations. As mentioned earlier, in such cases we applied either the existing global evidence or proxy national data, or estimated the values in consultation with local experts.

## Results

The results below reflect the model projections of the impact of baseline and the above four hypothetical scenarios on the course of the epidemic, burden on the health system and mortality in Kyrgyzstan. The model assumes that the vaccination in all hypothetical scenarios starts on July 1, 2021, thus, the potential changes in the epidemic are projected starting from this period.

### New daily reported and estimated unreported cases

As shown in Figure 3B, prioritizing the high-risk groups (50-64, and 65+ years old) for the vaccination significantly decreases symptomatic and laboratory confirmed cases in all scenarios. The improvement of mask wearing and social distancing (scenario 2 and 4) may

A) B)

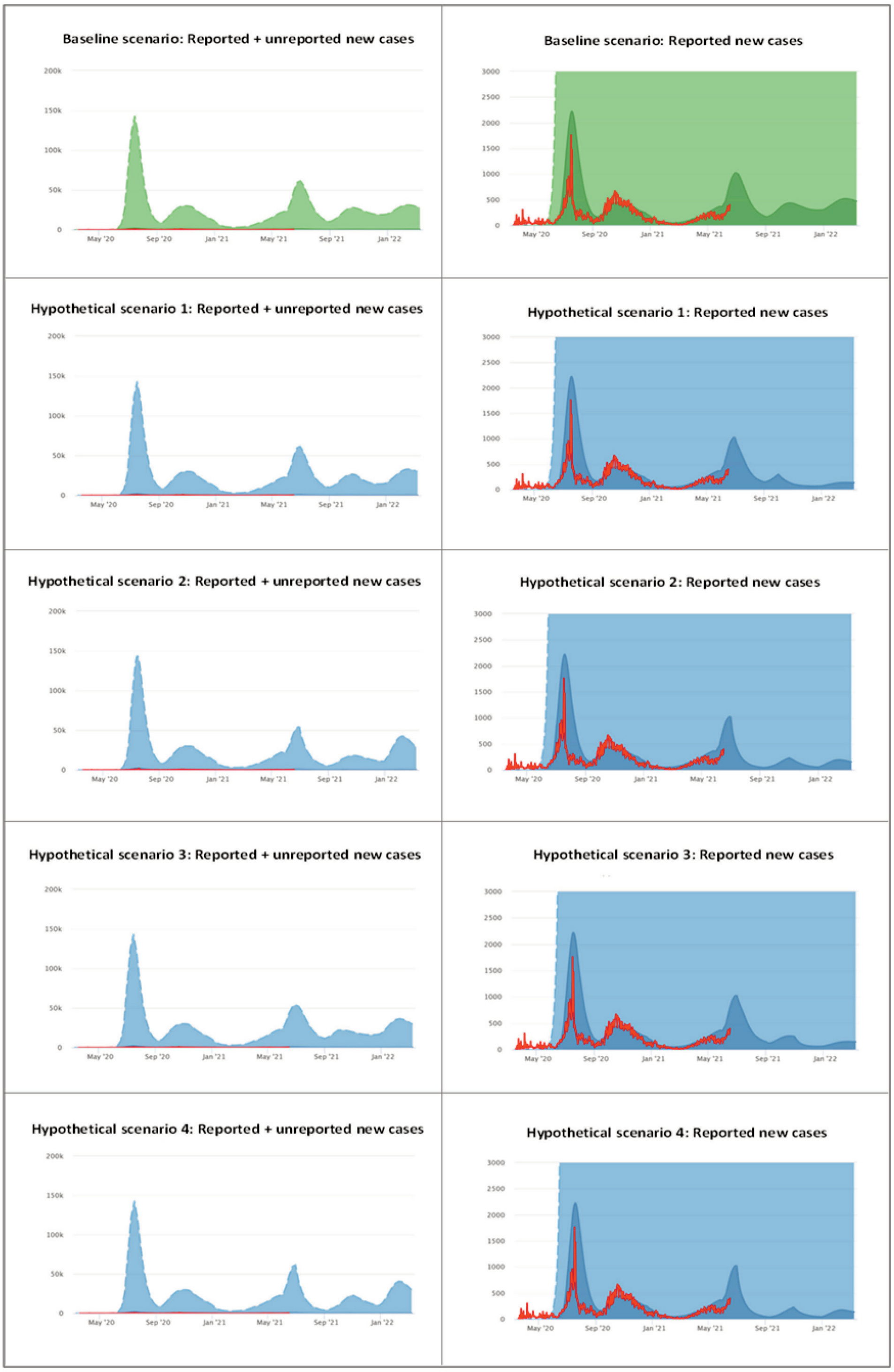



**Figure 3. Baseline and hypothetical scenarios (1-4) of projected new daily reported and unreported cases. Actual new daily reported cases (red curve).**

accelerate the decrease of new cases in the current wave and flatten the peaks of potential subsequent waves compared to alternative scenarios with baseline NPIs (scenario 1 and 3).

However, the small coverage of high-incidence groups (20-49 years old) does not significantly change the volume of unreported and asymptomatic cases in all scenarios (Figure 3A), though the inclusion of improved two NPIs slightly reduces the peak of the next potential wave in October 2021 with an increase of the potential

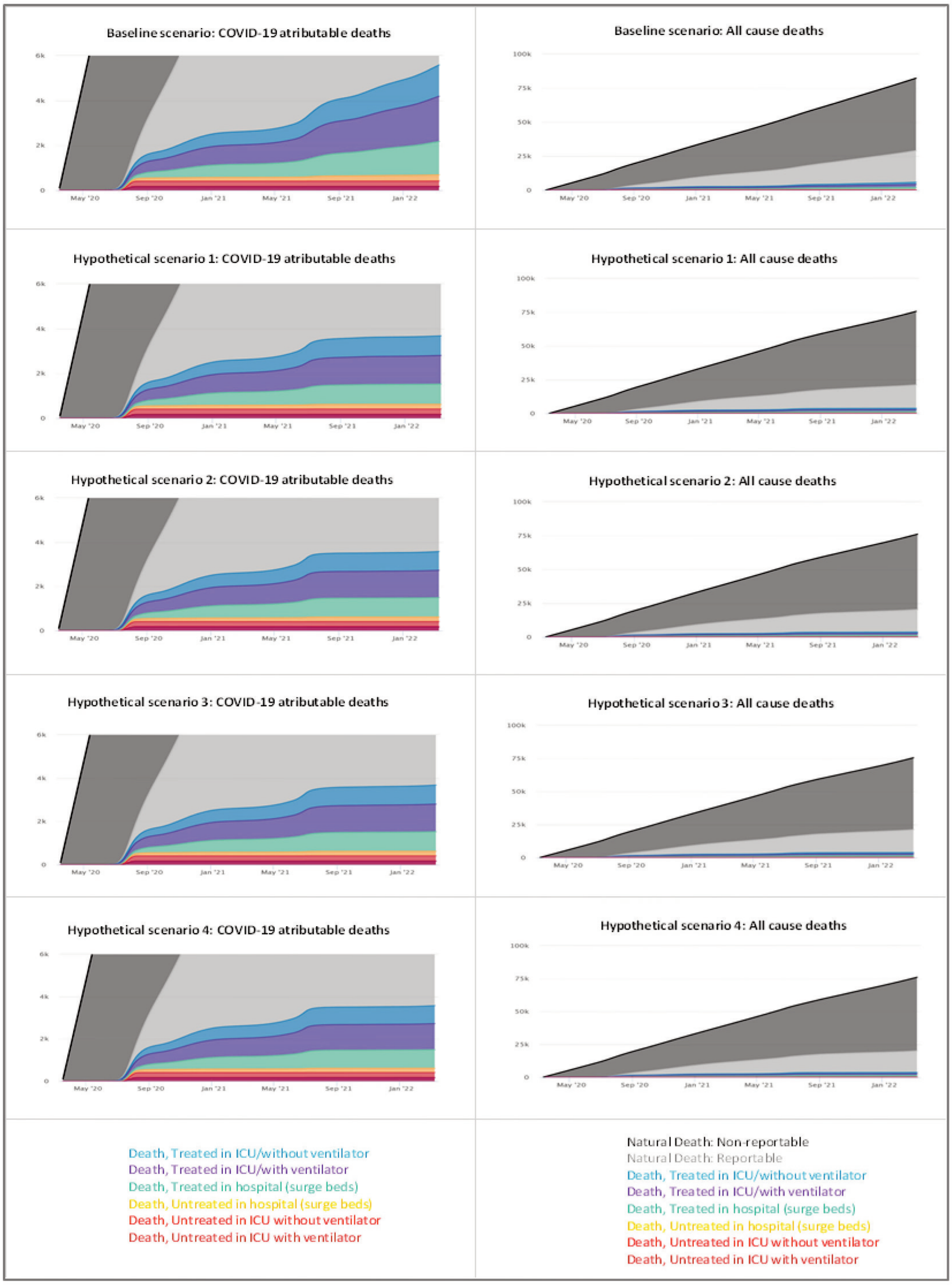



**Figure 5. Baseline and hypothetical scenarios (1-4) of projected COVID-19 attributable deaths and all-cause mortality.**

wave in February 2022 assuming that the indicated volumes of the vaccination will be completed by the end of the current year and no other roll-out will be expected after that. In addition, as with reported cases, the improved NPIs may also accelerate the reduction of new unreported cases in the current wave.

## Mortality

The model predicts that at the current level of NPIs and without vaccination (baseline scenario), the number of COVID-19 attributable deaths will reach 7,700 cases by the end of the model simulation period.

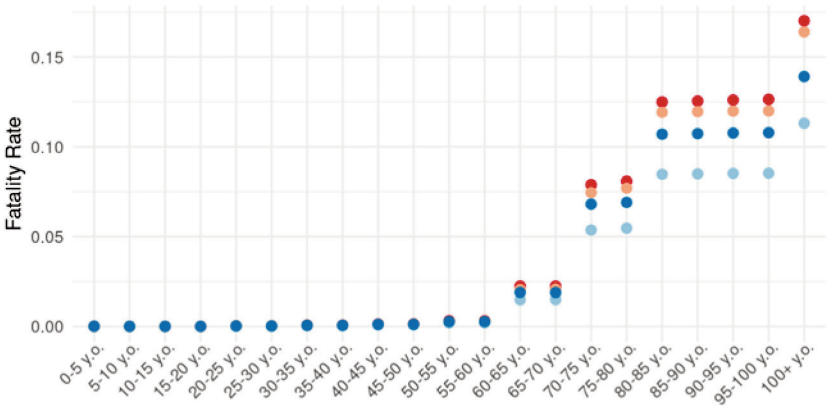



**Figure 6. CFR change during the course of the epidemic.**

Vaccination and the followed reduction of the pressure on the health system, will decrease the number of COVID-19 attributable deaths. As shown in Figure 5, the curve of the cumulative mortality of treated and untreated patients will flatten after the launch of the vaccination (all hypothetical scenarios).

The vaccination alone (scenarios 1 and 3) may reduce the number of deaths by 2040 – 2260 cases respectively, and in combination with improved mask wearing and social distancing (scenarios 2 and 4), it may decrease the mortality by 2480- 2500 cases relatively. In all scenarios, the patients aged 65+ years old will constitute the majority of COVID-19 related deaths (about 75%), followed by those aged 50-64 years old (about 17%). This trend may be explained by the preliminary higher CFR in these age groups with a further increase during intensive phases of the epidemic (Figure 6).

The vaccination with improved NPIs may decrease all-cause mortality from 27,000 cases (baseline) up to 16,000 (scenario 4), since hospitals and wards rearranged for COVID-19 patients will resume their work on preliminary designation (Figure 5).

## Discussion

This study suggests a potential positive impact of age-specified vaccination in reducing the level of symptomatic cases, burden on the health system and mortality in the short-term horizon. According to the model, prioritization of high-risk groups may help in reducing the COVID-19 attributable mortality and will potentially have an indirect positive effect on declining the deaths from other reasons as a result of lessened burden on the health system.

It should be noted that the national health system, already deteriorated in the last 30 years, experienced a tremendous pressure during the course of COVID-19 epidemic. As in many other countries with limited resources, during the intensive phases of the epidemic, most of available medical and human resources were rearranged and allocated to treat COVID-19 patients. In result, the MoH reported about 6430 cases of excess mortality (19.2%) in 2020, the majority of which were attributable to cardiovascular, COVID-19, lung diseases, followed by other causes (34,35). Accordingly, the decrease of the number of COVID-19 patients may improve the current situation in other health areas.

On the other hand, considering the fact that the population in Kyrgyzstan is young, the primary focus of the vaccination on high-risk groups with lower coverage of the people of younger ages may have less effect in reducing the incidence level. Thus, the herd effect in delaying another peak may only be achieved by reaching high-incidence groups more broadly.

Moreover, the model predicts that stopping of the vaccination after reaching the indicated coverages will later trigger a wave equivalent to the baseline scenario since the majority of the population will still not be protected and the spread will continue.

And finally, the model suggests that the lower vaccination coverage with improved NPIs may have a comparatively similar effect as the increased vaccination coverage with basic NPIs. In this model we increased the coverage for mask wearing and social distancing only, as they are considered as less disruptive interventions compared to school closure or working from home. Apparently, the combination of comparatively less disruptive interventions with vaccination may improve the effect from the vaccination. Considering the fact that most countries with limited resources are not likely to receive enough vaccine supply in the nearest future (1,36), such approach could be of benefit for controlling the epidemic, at least in a short-term perspective.

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