Alternative Vaccination Politics

Davide Manca (davide.manca@polimi.it)
Politecnico di Milano Dipartimento di Chimica Materiali e Ingegneria Chimica Giulio Natta
https://orcid.org/0000-0003-2055-9752

Lorenzo Benincasa
Politecnico di Milano Dipartimento di Chimica Materiali e Ingegneria Chimica Giulio Natta

Research

**Keywords:** Vaccination priority, Italy and Lombardy vaccination, Covid-19 vaccination simulator, Saved lives, Vaccination efficiency, Administration policies.

**DOI:** https://doi.org/10.21203/rs.3.rs-645859/v1

**License:** This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License
Alternative Vaccination Politics

Davide Manca*, Lorenzo Benincasa

PSE-Lab, Process Systems Engineering Laboratory
Dipartimento di Chimica, Materiali e Ingegneria Chimica “Giulio Natta”
Politecnico di Milano
Piazza Leonardo da Vinci 32, 20133 Milano, Italy

Prepared for “International Journal for Equity in Health”

First submission: June 20th, 2021

Copyright © 2021 Davide Manca, Lorenzo Benincasa

UNPUBLISHED
No parts of this paper may be reproduced or elsewhere used without the prior written permission of the authors

*Corresponding author: phone +39 02 23993271 fax: +39 02 23993280
e-mail: davide.manca@polimi.it
website: http://pselab.chem.polimi.it/
Abstract

**Background:** The timely implementation of the vaccination campaign and sharp rules for vaccine administration can make a difference. The paper investigates the impact of alternative policies based on scientific vaccination priorities inspired by the extended statistics on Covid-19 fatalities.

**Methods:** In the case of Covid-19 vaccination, a principal role is played by promptly adopting a reverse-order of age approach (to target first the elderly) coupled to covering the high priority categories but postponing the low priority ones. We implemented an in silico vaccination simulator capable of comparing what happened in reality with what might have happened if alternative vaccination policies had been adopted. The immunization profile and the death distribution curve allowed measuring the distance between reality and alternative policies and finally quantifying the expected number of saved lives.

**Results:** The alternative approach to vaccination was applied to Italy and Lombardy that host 60 and 10 million residents respectively. In about 100 days of vaccination based on (a) a reverse-order of age policy (from 90+ to 80-89 to 70-79 year-olds, etc.), (b) vaccination of priority categories, (c) postponement of non-priority categories and reallocation of such doses to (a) and (b), the saved lives would have been 3969 in Italy (of which 799 in Lombardy). In the same period, Italy suffered 30,911 fatalities (of which 5,613 in Lombardy). Of those fatalities, about 12.8% in Italy and 14.2% in Lombardy might have been avoided if a different approach to vaccination had been applied. Even better results would have been achieved if the elderly vaccination had been anticipated a few days (which started only 53 days after the very beginning of the Italian vaccination campaign) or if the vaccination engine had performed better in terms of daily administered doses while respecting the available delivered doses.

**Conclusions:** A different approach to the vaccination politics based on sharp and straight policies based on scientific quantitative data of Covid-19 mortality as a function of age and comorbidities would have accomplished a better quantitative effect on extinguishing the pandemic and containing the fatalities toll.

**Keywords:** Vaccination priority; Italy and Lombardy vaccination; Covid-19 vaccination simulator; Saved lives; Vaccination efficiency; Administration policies.
1 Background

A recent report from ISS, the Italian Superior Institute of Health, informs that 99% of the deaths since the very beginning of the Covid-19 pandemic involved over 50-year people (Italian Superior Institute of Health, 2021). Table 1 shows that deaths in excess of 85.6% consisted of over 70-year individuals.

Table 1: Statistics of the 118,589 Italian fatalities registered from the start of the pandemic (24-Feb-2020) to 28-Apr-2021 (Italian Superior Institute of Health, 2021). Data are organized in 10-year age ranges. $F(i)$ are the fatalities of the $i$-th age range. $F_{100k}$ are the fatalities of the $i$-th age range per 100,000 inhabitants. $R(i)$ are the sequential ratios of $F_{100k}$. $P(i)$ are the cumulative products of $R(i)$, with $P(1) = 1$.

| Age range [y] | Fatalities at 28-Apr-2021 | $F(i)/F(i-1)$ | Fatalities percentage | Italian inhabitants | Fatalities every 100,000 inhab | $R(i) = F_{100k}(i) / F_{100k}(i-1)$ | $P(i) = R(i)*P(i-1)$ | Percentage of deceased inhabitants |
|----------------|---------------------------|----------------|----------------------|---------------------|-------------------------------|-----------------------------------|---------------------|----------------------------------|
| 0-9            | 10                        | 0.0084%        | 4,892,494            | 0.20                | 1.0                           | 0.00020%                          |                     |                                  |
| 10-19          | 14                        | 1.4000%        | 5,706,116            | 0.25                | 1.2004                       | 1.0                              | 0.00025%                         |                                  |
| 20-29          | 59                        | 4.2143%        | 6,084,382            | 0.97                | 3.9523                       | 1.2                              | 0.00097%                         |                                  |
| 30-39          | 213                       | 3.6102%        | 6,854,632            | 3.11                | 3.2045                       | 15.2                             | 0.00311%                         |                                  |
| 40-49          | 1,016                     | 4.7700%        | 8,937,229            | 11.37               | 3.6584                       | 55.6                             | 0.01137%                         |                                  |
| 50-59          | 4,019                     | 3.9557%        | 9,414,195            | 42.69               | 3.7553                       | 208.9                            | 0.04269%                         |                                  |
| 60-69          | 11,728                    | 2.9181%        | 7,364,364            | 159.25              | 3.7304                       | 779.1                            | 0.15925%                         |                                  |
| 70-79          | 29,488                    | 2.5143%        | 5,968,373            | 494.07              | 3.1024                       | 2417.2                           | 0.49407%                         |                                  |
| 80-89          | 48,624                    | 1.6489%        | 3,628,160            | 1340.18             | 2.7125                       | 6556.8                           | 1.34018%                         |                                  |
| 90+            | 23,418                    | 0.4816%        | 791,543              | 2958.53             | 2.2076                       | 14474.6                          | 2.95853%                         |                                  |

The Covid-19 vaccination campaign started on December 27th, 2020 in Italy. The first eight weeks saw a vaccination rate of no more than 100,000 doses/day. The administered doses grew up to an average of 180, 250, 350, and 500 thousand doses/day every other four weeks respectively (Italian Ministry of Health, 2021). By mid-May 2021, Italy could administer a sustained rate of half a million doses/day. That value depended on both vaccine availability, vaccination capability, and vaccination adherence spread over the 21 regions and autonomous provinces of Italy. Italian regions are rather dissimilar in terms of morphology, population, area, and cultural background. These characteristics play a role in the vaccination campaign and adherence by the Italian population. Val d’Aosta is the least populated Italian region with 125,666 citizens and a density of 39 inhabitants per square kilometer. Lombardy is the most populated region with 10,060,000 inhabitants (which are one-sixth of Italy) and a density of 422 inhabitants per square kilometer (Italian Institute of Statistics, 2021). Indeed, Lombardy features a comparable number of citizens as Sweden, the Czech Republic, Greece,
Hungary, and Portugal but is significantly more populated than Israel, Austria, Switzerland, Denmark, Norway, Finland, Slovakia, Slovenia, Serbia, and Croatia. The large number of citizens in Lombardy made the vaccination campaign challenging and the high population density was a key factor together with the towering gross-domestic-product (i.e. industrial activity, travels, and commercial exchange) for the widespread and vast consequences played by Covid-19 in terms of infections, hospitalizations, and deaths (Bignami et al., 2021). Consequently, Lombardy was one of the Italian regions that most adhered to the vaccination campaign.

Italy is a republic and regions do not have significant political independence. Indeed, nationwide rules for vaccine administration characterized the initial phase of vaccination. However, several regions introduced further degrees of freedom as a function of local political pressures, the efficiency of their booking system, and the arrangement of the vaccination sites.

For the sake of clarity, the Italian vaccination campaign was organized into different population categories and age ranges.

Vaccinations were carried out locally, which means that every region according to the number of available vaccines, the vaccination adherence, and the number of citizens belonging to categories and age ranges achieved different vaccination rates and coverages. It is worth adding that Italy, as a member state of the European Community, received over 33 million doses by the end of May 2021 of four different vaccines: Janssen (2.2%), Moderna (9.2%), Pfizer/BioNTech (67.1%), and Vaxzevria (AstraZeneca) (21.5%). Unfortunately, the very rare adverse reactions after AstraZeneca’s vaccination played a significant role in the population acceptance of the vaccination campaign, and the residents of some Italian regions showed a noteworthy reluctance against that vaccine. In addition, at the end of March 2021, the Italian health ministry suspended Vaxzevria administrations for four consecutive days, which had repercussions of about 2-3 weeks to restore the scheduled vaccination rate.

For more than 50 days, since the start of the vaccination campaign, Italy chose to cover first some categories instead of prioritizing the population by a reverse-age approach. The main initial reason behind that decision was to immunize hospital personnel. However, besides medical doctors and nurses working in hospitals, the campaign involved also socio-sanitary personnel, technical, maintenance, security, and administrative personnel (both front- and back-office employees), medical students, psychologists, as well as hospital cleaners, bartenders, and gardeners. All the different ages (i.e. from 16 to 90+ years old) of those categories were covered, which induced a fierce debate on the ethical correctness of such prioritization (Craxì et al., 2021; Giubilini et al., 2021;
Williams et al., 2021). Two further critical categories were spotlighted: nursing home guests and fragile subjects. In addition, school/university personnel and armed forces received the vaccination before elderly people, thanks to the pressure of a few influential stakeholders. Unevenly, regions vaccinated also some peculiar subcategories that were lumped under the “other” category, for instance, lawyers, scientific informants, social workers, customs and airport personnel, and funeral home staff. Putting non-critical categories before the elderly caused further divisions among the persons in charge of the vaccination policies and highlighted the disparities among regions. A political change in the Italian government, together with the appointment of a new special pandemic commissioner on 1-Mar-2021 (at day #65 of the vaccination campaign), allowed straightening up the vaccination politics with a clear directive towards a reverse-age prioritization. Since mid-February 2021, people aged over 80 (more than 4.4 million in Italy) became the principal target. The vaccination politics then progressively focused on younger citizens, i.e. seventy year-olds, sixty year-olds, and so on by reverse order of age ranges (ROAR).

Again, regions did not start in unison. Lombardy was one of the slowest to open and implement the vaccination campaign for those over 80 and suffered a significant delay mainly due to a suboptimal booking system, which eventually was reworked. Lombardy took 75 more days to establish the Italian record of vaccinations with more than 116,800 doses administered in a day (vs 546,700 in Italy), well above (21.4%) the proportional percentage of regional vs national population (16.7%). However, it was not possible to sustain that vaccination rate due to the reduced availability of delivered doses. The following month of May 2021, Lombardy could afford an average of 85-90,000 doses/day, in line with the expected Italian target of half a million daily doses, which was also consistently attained.

2 Methods

2.1 An alternative approach to vaccination

The history of implementation of the Covid-19 vaccination in Italy is known and available in detail. Since the first day, the Italian ministry of health, through the special pandemic commissioner, publishes daily the vaccination data on a GitHub data repository (Italian Special Pandemic Commissioner, 2021) that provides an in-depth vision of both the delivered and administered doses. The delivered doses are detailed for each region in terms of vaccine brand and delivery date. The
administered doses are detailed for each region according to the vaccine brand, gender, age-range, category, and first/second dose. The categories are ten: health workers, non-health hospital workers, nursing home guests, fragile subjects, school/university personnel, armed forces, over-80, 70-79 years old, 60-69 years old, and others. The age ranges are 9: 16-19, 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, 80-89, 90+ years old. It may seem that there are overlaps between some categories and some age ranges, such as the 60-69 years old category and the 60-69 age range. Indeed, these values do not overlap as the age range includes all the citizens that were vaccinated and do not necessarily belong to the general-purpose category of 60-69 years old individuals as they may belong to other specific categories such as medical doctors, fragile subjects, teachers/professors, or armed forces personnel. Consequently, the vaccines administered to the 60-69 age range are more than those administered to the 60-69 category. The same goes for the 70-79 and over 80 categories, which are a subset of the 70-79 and (80-89 + 90+) age ranges.

Given the real account of Italian vaccination, a question arises spontaneously: could we have done better? What about different approaches to prioritization in terms of better immunization performance of the system?

These questions refer to three distinct points: (i) what alternatives, (ii) what priorities, (iii) what performance indicators. A further point (iv) needs to be defined to accomplish the performance assessment. This calls for assigning the rules and boundary/initial conditions to make the comparison fair and consistent.

About point (iii), i.e. the performance indicators, it should go without saying that the fatalities number is the first and foremost indicator capable of measuring the real success of the vaccination campaign. The four Covid-19 vaccines administered in Italy are reported to have an efficacy of 100% in preventing the hospitalization of an infected person (Anand and Stahel, 2021; Benenson et al., 2021; Olliaro, 2021; Vasileiou et al., 2021). Since the second wave of Covid-19, which started in Italy at the beginning of October 2020 (as of May 2021, Italy is experiencing the deflation trend of the third wave, which started towards the end of February 2021), Covid-19 patients die only in hospitals (Ciminelli and Garcia-Mandicó, 2020). For the sake of clarity, people do not die anymore at home or in nursing homes. Therefore, if the vaccine zeros the probability of being hospitalized and since patients may die only in hospitals, a reasonable assumption is that the vaccine zeros the probability of passing away. A further consequence of vaccination is that it transforms a deadly pandemic into a more manageable disease.
About point (i), the alternatives might have been to anticipate of some days the vaccination of some specific critical categories, to increase of some percentage points the number of daily vaccinations, to avoid the dispersion/dissipation of doses to less critical individuals as the ones reported in the Introduction.

About point (ii), conceivable priorities might have been (a) to avoid the vaccination of very young people even if they belonged to prioritized categories, (b) to go for a vaccination policy based on ROAR and assume it as the leading one.

Point (iv) calls for a consistent and fair approach to the alternative vaccination politics. We assume that all the simulations of alternative administrations should respect a few constraints: the delivered vaccines in terms of daily and regional availability, and number and brand of doses without any anticipation of what is expected to happen but is not yet fully accessible/regulated. This includes avoiding any a posteriori assumption based on historical data. The doses must also be administered respecting the present rules (that may change at either a regional or a national level during the vaccination campaign) in terms of age range accessibility and the interval between the first and second dose (except Janssen that is a single-dose vaccine). For the sake of clarity, the “age range accessibility” term refers mainly to the Vaxzevria vaccine that underwent a few changes in the Italian administration directives. As the vaccination campaign progressed, the Vaxzevria vaccine was prescribed to under 55, then under 65, then over 60 individuals, then tolerated for under 60, and finally forbidden for the under 60 year-olds (Faranda et al., 2021; Wise, 2021). However, these rules were not strictly respected and few citizens received Vaxzevria even though they were well over 80 years old during the periods when it was prescribed first to under 55 and then to under 65 year-olds (we are not able to explain why it happened). As far as the timespan between two doses is concerned, the Italian vaccination campaign adopted for more than 130 days in a row the following intervals: Pfizer/BioNTech and Moderna 21 days, Vaxzevria 70-84 days. Some regions firmly implemented the 70-day interval for Astra Zeneca (e.g., Lombardy), some others were more flexible and allowed citizens to book the first vaccination day and choose the second one within the 70-84 days timespan. In addition, when it came to “younger” age ranges, some regions (e.g., Lazio) allowed the citizens to book their preferred vaccine. This caused an overbooking of Pfizer/BioNTech and Moderna vaccines due to the biased opinion of a large portion of citizens mostly against the Vaxzevria vaccine and to a lesser degree the Janssen one. In some regions (e.g., Veneto) the selection of the vaccine was “indirect” as, by choosing the place were to be vaccinated, the citizens could become aware in advance of the vaccine brand that would be administered. On the contrary,
some regions (e.g., Lombardy) assigned the first (and second) date(s) and the vaccination site once the citizen had expressed their adhesion to the vaccination campaign. In Lombardy, the medical doctors at the vaccination site decided on the vaccine brand after an in-depth analysis of citizens' features and (co)morbidities.

2.2 Prioritization

When it comes to proposing an alternative approach to vaccination prioritization, one might be distracted by first paying attention to those who are either more exposed, or more productive, or more contagious with the target of mitigating the virus spreading and enhancing the national productivity (e.g., GDP) (Pardhan and Drydakis, 2021; Sarkodie and Owusu, 2021). However, the most important indicator is the death factor that focuses the attention on simply protecting and saving those who are more fragile and risk their lives. Targeting first those who are more fragile to the virus fulfills the highest ethical values that a democratic and fair society should be inclined to. Relatedly, in the case of an opposite approach based on either sub-ethical or unethical values determined by a selfish and opportunistic attitude, targeting first those who are more fragile to the virus is still the winning approach. Indeed, the reduction of the death count allows loosening the lockdown measures that are incompatible with the economic targets and the desire to live a fully realized and unconstrained life. Unfortunately, the Covid-19 pandemic has brought out orthogonal values that span from very altruistic principles to very selfish behaviors. Somehow, the preservation and defense of those who are most fragile to the virus are key factors that meet the values and interests of those conflicting categories of people.

Therefore, to preserve and defend the most fragile individuals, one has to minimize their probability of death. People may die if they are fragile because of their compromised physical condition or because of their age (as shown in Table 1). Indeed, the elderly are usually affected by comorbidities that increase the probability of fatality in the case of SARS-CoV-2 infection (Italian Superior Institute of Health, 2021). The older the age, the higher the probability of being affected by a greater number of comorbidities. In addition, the organs’ efficiency decreases significantly with age as well as the immune system's capacity to react to external solicitations (Grubeck-Loebenstein, 1997). These observations lead to identifying the main prioritization criterion simply based on vaccinating first the elderly and the nursing home guests.

Then a dilemma opens about the category of health workers that involves but is not restricted to medical doctors and nurses. One might propose to adopt the same reverse-age approach to that
category. However, many reasons urged vaccinating that category first. Among the cogent rationales, it is worth listing (a) the necessity to reduce/avoid infectious outbreaks in hospitals and the contagion of patients by medical staff; (b) to increase the number of available doctors, nurses, and biologists in the key analysis labs, intensive care units, and pneumology departments of hospitals; (c) to test, train, and tune the vaccination engine on a specific category of individuals who are intrinsically ready to face possible side effects and make experience by vaccinating each other; (d) acknowledge the prolonged sacrifice and dedication of both hospital and health workers and reduce the contagion risk that allows enhancing the quality and efficacy of their work. In the long run, the decision of creating a self-contained bubble of protected health workers allowed providing a better hospital service and quickening the progressive return to elective medicine.

2.3 Questions and open points

Several questions can be formulated under the umbrella of an optimal vaccination campaign. For instance, what would have happened if:

1. We had strictly administered in reverse-age order the doses that went to non-priority categories?
2. The vaccination campaign to the elderly (i.e. over 80 years old) had started 10 or 20 days before what happened in reality?
3. The daily vaccinations had increased by 10 or 20%?

It is worth underlining that these three points comply with the assumption that the administered doses respect the daily availability and the vaccination capacity of each Italian region.

Point (1) is based on the following hypotheses: (a) the non-priority categories are non-health hospital workers, school/university personnel, armed forces, and others; (b) the priority categories are health workers, nursing home guests, and fragile subjects; the remaining categories: over-80, 70-79 years old, and 60-69 years old are abandoned and substituted by ROAR (i.e. 90+ first, then 80-89, then 70-79, and so on).

Point (2) is motivated by the fact that in most of the Italian regions the vaccination of the elderly started very slowly and with significant delays. For instance, a large number of over 80 citizens in Lombardy received the first administration more than 55 days after having applied to the vaccination campaign. In addition, the Lombardy booking system for the over 80 was postponed and initially full of bugs.
Point (3) draws inspiration from what the vaccination engine might have accomplished (in terms of saved lives) if the whole supply chain had achieved a higher efficiency (in terms of daily administered doses). For the sake of clarity, we would like to inform the workers involved in the vaccination campaign of the increase in saved lives after an intensification of their contribution, in terms of either overtime or higher efficiency in the whole vaccination supply chain. To be even clearer, is the effort increase worth the achievable result? If the answer were affirmative then it would motivate the personnel involved in the vaccination engine to perform better and longer for the sake of a superior ideal. Unfortunately, the Italian vaccination engine performed in a suboptimal way regardless of the doses’ availability.

Figure 1: Daily administrations of Covid-19 vaccines from the first day 27-Dec-2020. The vertical grids are centered on Sundays. The dashed black horizon segments show the weekly vaccination averages. Left axis percentage of the half-million target, right axis number of vaccinations.

Figure 1 shows how the Italian vaccination campaign was characterized by a weekly periodicity. The reader can observe the so-called frog jump trend that repeats every seven days. The grid of Figure 1 is centered on Sundays and shows how the weekend days (i.e. Saturdays and Sundays) underperform with a decreasing trend in comparison with the maxima on Thursdays and Fridays. This weekend’s underperformance may be justified by the fact that the whole vaccination supply chain should periodically take a breath to deliver a sustainable and prolonged service. However, it is less clear why the working days see a monotonically steep increase from Mondays to
Thursdays/Fridays. Specifically, the first working days of the week underperform and it often happens that the administered doses on Mondays, Tuesdays, and Wednesdays are significantly less than those on Thursdays, Fridays, and Saturdays.

2.4 The vaccination simulator

The quantification of the differences discussed in Section 2.3 calls for a simulator of the vaccination campaign capable of implementing the real input data recorded in the different regions of a specific nation (e.g., Italy with its 19 regions and 2 autonomous provinces) and accepting dissimilar and flexible hypotheses of doses allocation to different categories and age ranges of the population that adhered to the vaccination campaign.

2.4.1 Recommended features

The recommended features and services of the vaccination simulator are:

- Download the input values from a data repository (e.g., GitHub) that is updated periodically (e.g., twice daily in Italy) and reports both administrations and delivered doses;
- Filter the input data and check for their consistency;
- (a) split the input data into separate regions/provinces, (b) organize the data chronologically, (c) arrange the tables (i.e. matrices) according to age ranges and categories, (d) activate boolean indicator(s) about first (and second) administration(s) as a function of the administered vaccine brand, (e) organize a chronological matrix with the delivered doses of vaccines and their corresponding brand;
- Import for each region/province and each age range the number of residents;
- Import the percentages of adherence to the vaccination campaign for each region and age range;
- Implement the possibly different administration rules (in terms of specific vaccines that either have to or do not have to be administered to certain categories or age ranges) enacted either at a national or regional level and that may change in time;
- Implement the key dates when the vaccination of specific priority/nonpriority categories took place at a national/regional level;
- Consider the vaccine features in terms of single or double administrations with the recall time in the case of two administrations.
The simulator engine loads all the input data reported above and must be able to allocate in different optimal modes the real administered doses that went to non-priority categories according to the ROAR approach discussed in Section 2.

The simulator relies on two further key features: the immunization profile (see Section 2.4.2) and the life-saving assessment (see Section 2.4.3).

### 2.4.2 Immunization profile

What does it happen to the human body when it receives the first and possibly the second dose of vaccine? We know that the immune system reacts to the exogenous input by developing antibodies that will fight SARS-CoV-2 infection (Mansourabadi et al., 2020). This reaction of the immune system is called immunization and makes a vaccine more or less effective against the virus infection. To our knowledge, the scientific literature does not report a quantitative law describing the dynamic profile of immunization after the Covid-19 vaccination. However, the literature reports some key values, times, and notes about most of the Covid-19 vaccines developed worldwide from which to infer a quantitative dynamic profile of immunization (Lombardi et al., 2021). Some papers report the degree of immunization in terms of the percentage of vaccinated individuals that were infected after they received either the vaccine or a placebo (Creech et al., 2021; Tenforde et al., 2021). These numbers are statistically collected through phase III clinical trials that entail two groups of volunteers that undergo a double-blinded vaccination campaign. Following the first and possibly the second vaccination shot, they lead a conventional life, may get in contact, and be infected by SARS-CoV-2. The ratio of infected volunteers who received the vaccine over those who received the placebo allows determining the vaccine efficiency in decreasing the probability of being infected after contagion (Chagla, 2021; Hall et al., 2021; Vasileiou et al., 2021).

Following the first administration, our body starts reacting and developing an antigen-specific immune response (specifically T and B lymphocytes, which produce antibodies in a rather complex biological cascade of mechanisms and transformations (Tufan et al., 2020)). The first maximum level of immunization is reached a few days later (Chagla, 2021; Knoll and Wonodi, 2021). At that time and in the case of two-dose vaccines, a second dose is administered. A few days later, the immune system reaches the maximum coverage (Kadire et al., 2021). We chose to adopt a conservative approach to implementing a functional dependency of immunization from time (i.e. the immunization profile) (Dan et al., 2013; De Bernardis et al., 2012; Le et al., 2014).
Figure 2: Immunization profile. The first administration occurs at $t_0$; $t_1$ is the induction time; at $t_2$ the first level $\alpha$ of immunization is achieved and the second (if any) dose is administered; at $t_3$ the maximum degree of immunization $\beta$ is reached and preserved for a few months.

As shown in Figure 2, we assumed that for few days (i.e. the induction time, $t_1$) after the first administration (which occurs at $t_0$) the immune system is capable of producing a negligible defense but that in the following days it triggers a suitable response that from zero (based on a conservative approach) increases linearly to the first $\alpha$ maximum value at time $t_2$. Usually, at $t_2$, the second administration for the two-dose vaccines occurs and a few days later, at $t_3$, a new maximum, $\beta$, is reached. Common values for $\alpha$ and $\beta$ are 0.7 and 0.95 respectively (Benenson et al., 2021; Chagla, 2021; Hall et al., 2021; Knoll and Wonodi, 2021). As anticipated in Section 2, $t_2 = 21$ d for Pfizer/BioNTech and Moderna, and $t_2 = 70-84$ d for Astra Zeneca with $\alpha = 0.7$ indifferently. In the case of Janssen, the one-dose vaccine, $t_2 = t_3 = 28$ d and $\alpha = \beta = 0.95$. For all the four vaccines we conservatively assumed $t_1 = 7$ d. It is worth adding that the scientific literature reports that the probability of getting into a serious infection after the immunization time, $t_3$, is negligible for all four vaccines administered in Italy (Chagla, 2021; Knoll and Wonodi, 2021). Articles inform that the probability of being hospitalized is almost zeroed after $t_1$ and that the immunity is supposed to last for 10-12 months (Fergie and Srivastava, 2021; Seow et al., 2020). These bits of information suggest assuming $\beta = 1$ as far as the death probability is concerned. At present, as discussed in Section 2, patients may die only in hospitals if seriously infected by SARS-CoV-2. Therefore, if the vaccine avoids any hospitalization then its efficacy can be assumed thorough ($\beta = 1$) against the risk of
death. For the sake of completeness, the immunization period of 10-12 months is much longer than the time horizon of the vaccination campaign and therefore we are authorized to keep $\beta$ constant for the whole simulation time (after $t_s$).

Specifically, the $t_3 - t_2$ interval is 7, 14, and 14 days for Pfizer/BioNTech, Moderna, and Vaxzevria vaccines respectively (Mansourabadi et al., 2020; Olliaro, 2021).

### 2.4.3 Life-saving assessment

To assess the efficacy of an alternative vaccination politics (and eventually make a comparison with the real vaccination campaign) it is necessary to calculate the number of deaths that would have occurred if that alternative politics had been implemented. The difference between the deaths occurred after either the real campaign or alternative politics measures the efficacy (if positive) or inefficacy (if negative) of the alternative vaccination politics. For the sake of clarity, the deaths still occurring after the real vaccination campaign (i.e. while it is carried out since it takes months to reach rather good levels of immunization) are available as they are registered daily (e.g., by the Italian civil protection department under the supervision of the Italian Ministry of health). In other words, the above-mentioned difference (if positive) coincides with the number of lives that the alternative vaccination politics would save.

To estimate the expected number of deaths in the case of an alternative vaccination politics, it is first necessary to quantify the number of vaccinated citizens, their immunization degree, and their age. The basin of people that may fall seriously sick and eventually die includes those individuals who have not yet reached a full immunization. Statistically, as we are dealing with large numbers of citizens (i.e. national/regional populations), we can consider the degree of immunization of those individuals who are progressively developing their immunity through the administration of the first (and possibly second) dose(s). We can calculate the dynamic percentage of immunization of the population of a region or a nation according to their age ranges and as a function of the administered doses.
Figure 3: Cumulated dynamic immunization of a susceptible population belonging to a specific age range of \( P \) cardinality. The green curve shows the evolution of the alternative vaccination politics, which prioritizes that specific age range (subject to all the constraints discussed in previous Sections). The blue line reports the degree of immunization achieved through the real vaccination campaign.

Figure 3 clarifies the rationale of the formulas that allow quantifying the number of lives that might be saved if the alternative vaccination politics were implemented. For the sake of simplicity, let us assume that Figure 3 refers to the 80-89 age range. The priority categories are respected and only the doses administered to non-priority categories are withdrawn and inoculated to the 80-89 year-olds. This vaccination starts at \( t_s \) as soon as the first withdrawn dose is available and any priorities by the older age range (i.e. 90+ years old) have been complied with. This means that first, all the 90+ years old individuals, who adhered to the vaccination campaign, receive at least the first dose. If the first dose administration to all the 90+ individuals takes less than \( t_s \) (in Figure 2) then the vaccination campaign to the 80-89 year-olds starts. At the same time, when the 90+ year-olds are ready for the second administration, the priority goes to them and only the remaining withdrawn doses go to the 80-89 year-olds. This priority cascade applies to all the age ranges in reverse order. Our simulations showed that the second administration priority to the different reverse order age ranges was always feasible (as far as the Italian regions and provinces are concerned).

It is worth spending a few words about point \( P \) of Figure 3, which is the number of citizens of that specific age range who live in the nation/region under study. For the sake of precision, \( P \) is the number of susceptible citizens i.e. the total number of residents less the individuals who either healed from Covid-19 or died. Indeed, even though Covid-19 plagued the elderly significantly, the
susceptible population can be merged with the resident population also because the vaccination
directives suggest that the healed individuals should nonetheless undergo the vaccination campaign
to stabilize and equalize their immunization degree (Gobbi et al., 2021).
The immunization degree of each age range depends on the specific adherence to the vaccination
campaign, which may vary significantly among regions. For instance, by the end of May 2021, the
population fraction that received the first administration was 43% in Molise and only 33% in Sicily.
Equally, the Lombardy citizens in their 90s who received the first administration were 99.97% and
90.88% had received the second shot. According to a more general approach to vaccination, both
the blue and green curves of Figure 3 (that depend on the degree of adherence to the real
vaccination campaign) reach distinct horizontal asymptotes that are lower than \( P \). Both the blue
and green lines at time \( t_i \) of Figure 3 are the summation of the fractional contributions to
immunization of each corresponding vaccinated individual whose immunization degree belongs to
the \([0, \beta]\) interval.
At \( t_i \), the number of citizens who are exposed to a possible contagion is either the segment \( AC \)
in the case of the real vaccination campaign or \( AB \) in the case of the alternative vaccination politics.
\( BC \) measures the distance between the alternative and the real vaccination campaigns and is
proportional to the number of lives that may be saved. The real number of fatalities \( (F^R_i) \) is known
at each day \( (t_i) \) and we can rely on the fatalities distribution by age ranges \( (k) \) reported in Table 1.
Therefore, we can evaluate the fatalities \( (F^A_i) \) that occurred every day for each age range. Finally,
the number of fatalities that might have occurred in the case of the alternative vaccination politics
every day for each age range can be determined from the following proportional law:

\[
F^A_{i,k} \cdot F^R_{i,k} = AB_{i,k} \cdot AC_{i,k}
\]  

(1)

It follows that:

\[
F^A_{i,k} = F^R_{i,k} \frac{AB_{i,k}}{AC_{i,k}}
\]  

(2)

If the vaccination campaign lasts \( ND \) days then the total number of fatalities that would have
occurred to all the \( NR \) age ranges in the case of both the alternative and real vaccination campaigns
are:

\[
F^A_{TOT} = \sum_{i=1}^{ND} \sum_{k=1}^{NR} F^A_{i,k} = \sum_{i=1}^{ND} \sum_{k=1}^{NR} F^R_{i,k} \frac{AB_{i,k}}{AC_{i,k}}
\]  

\[
F^R_{TOT} = \sum_{i=1}^{ND} F^R_{i,k}
\]  

(3)
Eventually, the number of lives that the alternative vaccination politics would save is:

$$N_{LS} = F_{TOT}^R - F_{TOT}^A = \sum_{i=1}^{ND} F_{i}^R - \sum_{i=1}^{NR} \sum_{k=1}^{ND} F_{i,k}^R \frac{AB_{i,k}}{AC_{i,k}} = \sum_{i=1}^{ND} \sum_{k=1}^{NR} F_{i,k}^R - \sum_{i=1}^{NR} \sum_{k=1}^{ND} F_{i,k}^R \frac{AB_{i,k}}{AC_{i,k}} = \sum_{i=1}^{ND} \sum_{k=1}^{NR} F_{i,k}^R \left( 1 - \frac{AB_{i,k}}{AC_{i,k}} \right) (4)$$

The green line in Figure 3 is not always higher than the blue one for any age range. Actually, the younger age ranges receive a minor knockback due to the doses withdrawn from the non-priority categories and administered according to ROAR. Since the daily doses are assigned according to the real administrations, the withdrawn doses have a minor negative impact on the younger age ranges but produce a major improvement on the older ranges. From a conceptual point of view, the younger categories may experience the following condition: $AB_{i} > AC_{i}$ at some $t$. Altogether, an alternative vaccination politics, to be successful, must obey the following condition: $N_{LS} > 0$.

### 2.4.4 Vaccination rules

The vaccination simulator has to comply with and implement a record of rules that are aimed at preserving the most fragile individuals and shorten as far as possible the achievement of their highest immunization degree. The following list reports the main vaccination rules:

- In the case of dose shortage, prioritize the second administrations;
- Prioritize the vaccines characterized by shorter $t_2$ times (as of Figure 2) to the older age ranges;
- Supersede the regional and wavering decisions about the Vaxzevria vaccine and equalize the administration for all the simulated regions starting from April 8th, 2021 (as it happened in Lombardia) to the 60-69 and 70-79 year-olds. For the sake of clarity, AIFA (the Italian Pharmacological agency) at the very beginning of the vaccination campaign prescribed the Vaxzevria vaccine only to under 55 year-olds. Later, the elderly were admitted to that vaccine;
- As a tightening rule, avoid the administration of Vaxzevria to those over eighty as it takes at least 70 days for the second administration;
- A consequence of the previous point is that people over eight-year receive only Pfizer/BioNTech and Moderna vaccines. The 70-79 year-olds may receive also Vaxzevria and Janssen;
- Assume that the fatality distribution with age ranges is constant in time and space (i.e. it does not depend on single regions/provinces as regional data are not publicly available). The time-constant hypothesis was extensively discussed in Section 2 and reported in Table 1).
• No vaccine mixing is allowed in the case of two-dose vaccines (this rule held in Italy throughout this study, which had to be stopped when the data about category vaccination were suddenly and unjustifiably removed from published data on 28-May. Only by mid-June a two-dose mixing of Vaxzevria and either Pfizer/BioNTech or Moderna vaccines was prescribed for the few under 60 year-olds who received the first dose of Vaxzevria);

• The first vaccination day to the elderly is assumed to be the fifty-fourth day (i.e. February 18th, 2021) from the start of the vaccination campaign (as it happened in Italy) when a good fraction of the prioritized categories had already been vaccinated;

• The following three categories: health workers, nursing home guests, and fragile subjects are priority categories and the alternative vaccination campaign cannot use any of the reserved doses that are administered to them;

• A consequence of the previous point is that a young citizen of those priority categories deserves vaccination as the elderly;

• The doses administered to the remaining seven categories (i.e. non-health hospital workers, school/university personnel, armed forces, over-80, 70-79 years old, 60-69 years old, and others) remaining categories are withdrawn by the alternative vaccination politics and redistributed according to the ROAR criterion;

• A consequence of the previous point is that the doses administered to the over-80 category are withdrawn and reassigned in reverse order to the 90+ and 80-89 age ranges;

• The citizens who received the first dose before the start of the alternative vaccination politics and are waiting for the second dose will be administered accordingly regardless they belong to non-priority categories.

2.4.5 Program implementation

We chose to implement the vaccination simulator in Matlab 2021a (The MathWorks Inc., Natick, MA, USA). Matlab is a rather practical prototyping tool (although it is not a real programming language) that can download and read remote data on the Internet, work with tables containing different data types (e.g., characters, strings, headings, date and time, integer, and floating-point values) organized in different file formats (e.g., JSON, CSV text files, and raw data). Matlab’s most interesting feature for the vaccination simulator is the data filtering option which can prune large tables and efficiently select the data that are necessary to comply with the rules reported in Section 2.4.4. In addition, Matlab can draw good-quality diagrams and figures, and produce reports for the
As far as the CPU efficiency is concerned, even though Matlab is an interpreted language and its efficiency is quite low, this is not a limiting feature as a single comparison between the real and the alternative vaccination campaign that covers all the 21 regions and autonomous provinces of Italy takes 50.5 s on an Intel i7-4600U processor running at 2.1 GHz with 16 GB of RAM (i.e. an ordinary Windows 7/10 notebook). In the case of Lombardy, the most populated Italian region, the CPU time is 14.4 s. The Matlab routines that simulate the alternative vaccination politics roughly consist of 2,500 lines of code.

3 Results and discussion

The basic comparison between the alternative vaccination politics (AVP) and the real vaccination campaign (RVC) refers to Italy with their contemporary start at 18-Feb-2021, when most of the vaccinations to priority categories had occurred. That was day #54 after the very beginning of the Italian vaccination campaign on 27-Dec-2020. Figure 4 and Figure 5 show the comparison for the most exposed and fragile age ranges (over 80 year-olds, and 70-79 year-olds) that cover most of the fatalities due to SARS-CoV-2 infection.
Figure 4: Comparison between the Italian alternative vaccination politics and the real vaccination campaign for the over-80 year-olds. The comparison covers a 99-day interval and the vertical grids are weekly spaced. The blue dashed line shows the adherence to the vaccination campaign by the over 80 year-olds.

Figure 5: Comparison between the Italian alternative vaccination politics and the real vaccination campaign for the 70-79 year-olds.

In the over 80 year-olds the AVP first and second administration doses (green lines) are always consistently above the RVC doses (red lines). This shows how the elderly did not receive enough attention and priority, and that a strict ROAR criterion was not respected. Specifically, Figure 5 confirms this statement as in the first nine weeks of AVP the real doses administered to 70-79 year-olds were withdrawn and primarily administered to older citizens (i.e. 90+ and 80-89 year-olds). The dose reallocation of AVP would have covered all the over 80 year-olds with the first administration six weeks earlier than reality. In addition, AVP would have been able to finalize the second administration to over 80 year-olds one/two weeks before the end of May and achieve an almost complete immunization by the end of May instead of the lesser RVC coverage. For the sake of detail, the enhanced vaccination coverage achieved by AVP does not rely only on withdrawing the improperly administered doses to the 70-79 age range but to all the younger age ranges that received any doses before the older ones were fully covered.
Focusing on the 70-79 age range, AVP is capable of crossing and surpassing RVC on 25-Apr as far as the first administration doses are concerned. As of 13-May, the AVP immunization level becomes higher than the RVC one. These results are achieved by a continuous and strict application of the ROAR criterion that withdraws systematically the doses erroneously administered to younger citizens in favor of the older ones.

The rate of administration of the second dose and the achieved immunization degree are further important points of discussion. Figure 4 and Figure 5 show the whole accomplishment of the second dose and immunization degree for the over 80 year-olds well before the end of May. The same does not happen in the case of the 70-79 age range. That is mostly due to the different brands of vaccines administered. Indeed, the over 80 year-olds received only Pfizer/BioNTech and Moderna vaccines (with 21 days between two doses) whilst the 60-69 and 70-79 age ranges received also a good amount of Vaxzevria vaccines (with 70 days between two doses). Negligible amounts of Janssen vaccine were administered (nonetheless, the vaccination simulator took into account every dose administered anywhere and at any time).

Figure 6: Number of lives that might have been saved if the alternative vaccination politics had been implemented in Italy instead of the real vaccination campaign. Blue line and left y-axis cumulated saved lives; green bars and right y-axis daily saved lives.
Figure 6 shows the results in terms of possibly saved lives that the AVP would have achieved in the simulated 99-day time horizon (from 18-Feb to 27-May-2021). Our simulation estimates that it would have been possible to save 3969 lives (of which 799 in Lombardy). In that period Italy suffered 30,911 fatalities (of which 5,613 in Lombardy). Of those fatalities, about 12.8% in Italy and 14.2% in Lombardy might have been avoided if a different approach to vaccination had been applied. These figures increase monotonically in time and will produce an even larger hiatus between what happens (RVC) and what might occur (AVP) and show how scrupulous and timely decisions based on informed directives can play a vital role in human lives.

A parallel discussion can be carried out in the case of a specific region, for instance, Lombardy. For the sake of space, we report only the diagrams of the 70-79 year-olds (see Figure 7) that are the most important and dissimilar when compared with the Italian equivalents. The distance between the green and red lines for the first dose is narrower for Lombardy than for Italy. Similarly, the regional second dose curves and the immunization trends are nearer than the national ones. This means that somehow the vaccination priority towards those above 70 was more preserved in Lombardy than in Italy. Nonetheless, the improvement in terms of saved lives that AVP would have achieved at the regional level is a little better than the national one as the total number of fatalities in Lombardy was proportionally slightly higher than in Italy.
Figure 7: Comparison between the alternative vaccination politics and the real vaccination campaign in Lombardy for the 70-79 year-olds.

Table 2 reports the most important deadlines and the percentages achieved by AVP in Italy and Lombardy. The Italian values refer to the whole nation, which means that they report what would have been achieved if the vaccination campaign had been carried out at a national level. Conversely, the vaccination campaign was managed regionally with national-level coordination in terms of vaccine brand recommendations to different age ranges, dose supply, and recommended daily/weekly/monthly administrations. Regions were independent in designing the administration supply chain, meeting the recommended administration rates, adapting the time interval between the first and second dose, anticipating some age ranges or specific working categories, allowing/forbidding the citizens to choose the vaccine brand, and first administration date and site. For the sake of detail, the dates reported in Table 2 do not consider the three priority categories that proceed independently and follow the RVC schedule. Conversely, the percentages refer to all the categories split into age ranges and allow grasping the whole picture of the vaccination campaign.

Table 2: Results of the alternative vaccination politics achieved in the 18-Feb to 27-May-2021 timespan (99 days) in Italy and Lombardy.

| Detail                                                   | Italy              | Lombardy          |
|----------------------------------------------------------|--------------------|--------------------|
| First dose start to the 90+ age range                    | 18-Feb (day #1)    | 18-Feb (day #1)    |
| First dose end to the 90+ age range                      | 01-Mar (day #12)   | 03-Mar (day #14)   |
| First dose start to the 80-89 age range                  | 01-Mar (day #12)   | 03-Mar (day #14)   |
| Second dose end to the 90+ age range                     | 22-Mar (day #33)   | 27-Mar (day #38)   |
| Full immunization date of the 90+ age range              | 04-Apr (day #46)   | 06-Apr (day #48)   |
| First dose end to the 80-89 age range                    | 15-Apr (day #57)   | 13-Apr (day #55)   |
| Second dose end to the 80-89 age range                   | 06-May (day #78)   | 04-May (day #76)   |
| Full immunization date of the 80-89 age range            | 19-May (day #91)   | 17-May (day #89)   |
| First administered dose of Vaxzevria vaccine to the 70-79 age range | 08-Apr (day #50) | 08-Apr (day #50) |
| First dose (other vaccines than Vaxzevria) to the 70-79 age range | 15-Apr (day #57) | 13-Apr (day #55) |
| First dose end in the 70-79 age range                    | 05-May (day #77)   | 30-Apr (day #72)   |
| Second dose end in the 70-79 age range                   | Not yet reached    | Not yet reached    |
| Full immunization date of the 70-79 age range            | Not yet reached    | Not yet reached    |
| Immunization percentage of over 80 year-olds             | 99.188%            | 99.475%            |
| Percentage of over 80 year-olds with the first administration | 100%              | 100%              |
| Percentage of over 80 year-olds with the second administration | 97.381%           | 97.637%           |
Table 2 allows comparing the performance of a single region to the whole nation. Indeed, we can observe that in the very first days of AVP, Lombardy is slower than Italy with the first administration to the 90+ and 80-89 age ranges. However, Lombardy regains and outperforms Italy when the second dose and full immunization of the 80-89 age range is concerned.

Figure 8: Different alternative vaccination politics in Italy as a function of the initial date. The red star and the green diamond lines show the expected saved lives if the vaccination had started respectively 10 and 20 days before the standard AVP that began on 18-Feb-2021 in Italy for the elderly, i.e. 54 days after the very first administration occurred on 27-Dec-2020.

Figure 8 shows what would have happened in terms of the Italian vaccination campaign if it had started either 10 or 20 days before the official date of the vaccinations given to the elderly. As discussed above, the first vaccination day for the over 80 year-olds was 18-Feb-2021, i.e. 54 days after the very first day of the vaccination campaign that was initially dedicated to some specific

| Vaccination campaign adherence of the 80-89 age range | 93% | 94.753% |
| Vaccination campaign adherence of the 90+ age range | 96.183% | 99.463% |
| Immunization percentage of over 70-79 year-olds | 66.318% | 64.872% |
| Percentage of 70-79 year-olds with the first administration | 100% | 100% |
| Percentage of 70-79 year-olds with the second administration | 52.536% | 47.571% |
| Vaccination campaign adherence of the 70-79 age range | 85% | 85.249% |
| Total saved lives by the alternative vaccination campaign | 3969 | 799 |
categories (unfortunately not all of them at high priority). If the vaccination to the elderly had started 10 days before (on 8-Feb) the saved lives at 27-May would have been 4466 (instead of 3969, i.e. an improvement of 12.5%). If the vaccination to the elderly had started 20 days before (on 29-Jan) the saved lives would have been 5317 (i.e. an improvement of 35.1%). The significant improvement of the 20-day over the 10-day politics is due to the significantly higher number of doses administered to non-priority categories that would have been withdrawn and inoculated to the elderly. January 2021 saw a high number of low-priority citizens vaccinated instead of the elderly, most of them being armed forces and non-health hospital workers. The question about the feasibility of starting the vaccination campaign for the elderly has an affirmative answer. The running-in of the vaccination campaign had already occurred and the booking system for ordinary citizens such as the elderly should have been deployed earlier and with more efficiency. Similar numbers may be reported for Lombardy, with 894 and 1123 lives saved (as of 27-May) if AVP had anticipated 10 and 20-day respectively. Compared with the 799 lives saved if AVP had started on 18-Feb, the improvement would have been 11.9% and 40.5% respectively.

Table 3: Saved lives in Italy by AVP. The rows of the matrix report the calculated saved lives under the hypothesis of administering the same amount (100%) or 10% and 20% more daily doses than those administered during RVC. The columns report the calculated saved lives under the three hypotheses of 0, 10, and 20 days anticipation of AVP compared to RVC (which started on 18-Feb-2021). The numbers in brackets quantify the increase over the basic case study of 18-Feb at 100% administrations.

| AVP – Saved lives – ITALY | Start on 18-Feb-2021 | Start on 8-Feb (10 days before) | Start on 29-Jan (20 days before) |
|--------------------------|----------------------|--------------------------------|---------------------------------|
| 100% of the RVC administrations | 3969 | 4465 (+12.50%) | 5317 (+33.96%) |
| 110% of the RVC administrations | 4905 (+23.58%) | 5414 (+36.41%) | 6311 (+59.01%) |
| 120% of the RVC administrations | 5712 (+43.92%) | 6245 (+57.34%) | 7083 (+78.46%) |

Table 4: Saved lives by AVP in Lombardy. See Table 3 for the details of rows, columns, and cells.

| AVP – Saved lives – LOMBARDY | Start on 18-Feb-2021 | Start on 8-Feb (10 days before) | Start on 29-Jan (20 days before) |
|-----------------------------|----------------------|--------------------------------|---------------------------------|
| 100% of the RVC administrations | 799 | 894 (+11.89%) | 1123 (+40.55%) |
| 110% of the RVC administrations | 963 (+20.53%) | 1059 (+32.54%) | 1299 (+62.58%) |
| 120% of the RVC administrations | 1109 (+38.80%) | 1205 (+50.81%) | 1417 (+77.35%) |

A further open point of AVP is about what would have happened if the whole vaccination supply chain had been more efficient than RVC. What would have happened if the daily administrations
had been 10% or 20% more than the real ones? First, it is worth underlining that these hypotheses are feasible in terms of available doses (i.e. delivered doses). This means that even a hypothetical increment of 20% of the daily administered doses would have complied with the real available doses at both national and regional levels. How one can achieve an administration increase of 10% or 20%? Such an increase would interest the whole vaccination engine that builds on the vaccination supply chain. One might work on either improving the efficiency of the engine or increasing the operation of that engine. On the one hand, the efficiency may be tuned and polished in several different ways but it has to deal with the so-called rate-determining step, which is the less efficient step of the engine, i.e. the bottleneck. On the other hand, the operation of the engine may be improved by increasing the time worked. The easiest way would be to introduce overtime. If one assumes that personnel works 8 hours per day an increase of 10% or 20% would call for 48 min and 96 min overtimes. From a practical point of view, personnel might be asked to work either 1 or 1.5 h more. The improvement in saved lives would be much more significant (as reported in Table 3 and Table 4) and would probably motivate the workers of the vaccination supply chain to embrace overtime with the promise of creating an impact on the number of saved lives. Indeed, the cause of the greater good (coupled with paid overtime) is something that may motivate workers to outperform. The positive results of AVP are evident and significant (as shown in the Figures and Tables of this Section). However, is AVP feasible or too optimistic and distant from reality? In our opinion, most of the hypotheses we introduced for AVP to occur are rather realistic and based on pragmatic assumptions. Nonetheless, we see two limitations.

The first limitation is probably the most severe and it deals with the strict ROAR hypothesis that would call for vaccinating first the 90+ and then the 80-89 year-olds and so on. This strict approach to the vaccination sequence of the elderly would call for a very robust engine capable of timely delivering the administrations to citizens who usually have to rely on the help of relatives and/or caregivers and who require a longer time for finalizing a single vaccination. In addition, the reduced time to promptly adhere to the vaccination campaign (to achieve an efficient ROAR approach) is a further and derived limitation of that proposed martial approach. Indeed, a longer time to convince the skeptics would better approximate what in reality happened.

The second limitation is that the algorithm used to determine the expected number of saved lives by AVP uses the daily real fatalities in the region/nation whilst the first and second administrations that contribute to the progressive degree of immunization of the vaccinated population have a delayed effect on the number of deaths. One might introduce a further adaptive parameter in
Equation (4) in terms of a time delay to better account for the infection, disease, hospitalization, and death chain. In our opinion, this alternative would introduce a further degree of uncertainty. That is why we intentionally used the daily fatalities to calculate the expected saved lives as a function of the immunization degree of the different age ranges at the same time of those fatalities. A final remark should be devoted to the possibility that the fatalities distribution as a function of age might dynamically change its profile according to the unbalanced vaccination coverage of the population. Reality showed that the percentage of elderly fatalities is not significantly affected by the vaccination campaign. This result might seem surprising and counterintuitive. In reality, the vaccination campaign produces the most important results in decreasing significantly the fatalities number. The elderly remain more exposed to life risk than young people and also minor numbers of non-vaccinated elderly still contribute at a large extent to the daily fatalities. This is a further demonstration that it is worth vaccinating the elderly at very high percentages and avoiding any reluctance.

4 Conclusions

How the real vaccination campaign has been carried out so far in Italy at both national and regional levels inspired and motivated this article. Could it have been better? The answer is a definitive yes. For the sake of correctness, Italian RVC might have been even worst. Indeed, in March 2021, the new special pandemic commissioner forced RVC to rigorously implement the inverse order of age ranges approach and set the half-million target of daily-administered doses. He stepped up the pressure on every single region of Italy to proportionally reach that target through scheduled weekly and eventually daily increasing values to be scored. As a matter of fact, this paper does neither want to blame nor to criticize the Italian vaccination campaign that at present is amongst the best in the European Community in terms of both administered doses and population coverage (European Centre for Disease Prevention and Control, 2021). We just wanted to show how a better knowledge and implementation of the vaccination policies together with an earlier start of the vaccination campaign specifically targeted to the elderly would have influenced significantly the fatalities restraint. The initial efficiency of the vaccination engine was rather low regardless of the preliminary and necessary running in. A not negligible amount of doses was administered to non-priority categories leaving the elderly exposed for a longer period to SARS-CoV-2 infection. Some of the over 80 years-olds took more than 100 days
before receiving the first dose. After 150 days since the very beginning of the vaccination campaign, quite a few over 80 year-olds were still receiving the first dose. This important delay in the finalization of the vaccination campaign to the elderly played a paramount role in the fatalities toll paid to the Covid-19 pandemic. Besides accelerating the vaccination of the elderly, the higher efficiency of the vaccination engine and overtime would have saved a higher number of lives. These are the lessons learned that may help future decision-makers in the case of new outbreaks towards the implementation of an enlightened vaccination politics. We intentionally used the term politics in this article instead of policy as the setting of a vaccination campaign under a pandemic emergency is more related to strategic political decisions rather than to tactical applied policies.

The availability of an in-silico vaccination simulator allows running a set of parametric simulations based on different scenarios, priority allocations, date shifts, and administration policies. For instance, it can be used to analyze the (in)effectiveness of increasing the time interval between the first and second dose of vaccines (e.g., from 21 to 35 or 42 days for the Pfizer/BioNTech or Moderna vaccines). However, this is another story that goes beyond the scope of this article. Finally, the in-silico vaccination simulator can be used for prediction purposes by assigning the expected future administration rates and estimating the upcoming fatalities with suitable predictive models (Manca et al., 2020).

**List of abbreviations**

| Abbreviation | Description |
|--------------|-------------|
| AVP          | Alternative Vaccination Politics |
| Covid-19     | CoronaVirus Disease 2019 |
| ISS          | Italian Superior Institute of Health |
| ROAR         | Reverse Order of Age Ranges |
| RVC          | Real Vaccination Campaign |
| SARS-CoV-2   | Severe Acute Respiratory Syndrome CoronaVirus 2 |
Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The data used in the paper are publicly available at:

1) GitHub repository: https://github.com/italia/covid19-opendata-vaccini
   Specifically:
   - https://raw.githubusercontent.com/italia/covid19-opendata-vaccini/master/dati/somministrazioni-vaccini-summary-latest.csv
   - https://raw.githubusercontent.com/italia/covid19-opendata-vaccini/master/dati/somministrazioni-vaccini-latest.csv
   - https://raw.githubusercontent.com/italia/covid19-opendata-vaccini/master/dati/anagrafica-vaccini-summary-latest.csv
   - https://raw.githubusercontent.com/italia/covid19-opendata-vaccini/master/dati/consegne-vaccini-latest.csv

2) ISTAT databank: http://dati.istat.it/

Competing interests

The authors declare that they have no competing interests.

Funding

None.
Authors' contributions

DM theorized and designed the alternative vaccination politics, devised and wrote the algorithms and the functional dependencies of immunization profile and saved lives, coded portions of the software, wrote the manuscript, and supervised the study.

LB coded portions of the software, implemented the dose reallocation rules, organized the database of age ranges for each Italian region, and read, revised, and approved the final manuscript.

Acknowledgements

The authors acknowledge the valuable contribution of Paolo Maggioni, Enrico Storti, Dario Caldiroli, Elena Bignami, Piergiorgio Villani, Giovanni Mistrarelli. DM acknowledges the fruitful discussions and comments of Giuseppe Pesenti.

References

Anand, P., Stahel, V.P. (2021). Review the safety of Covid-19 mRNA vaccines: a review. Patient Safety in Surgery, 15.

Benenson, S., Oster, Y., Cohen, M.J., NirPaz, R. (2021). BNT162B2 mRNA COVID-19 vaccine effectiveness among health care workers. New England Journal of Medicine, 384, 1775-1777.

Bignami, E., Manca, D., Bellini, V. (2021). Riding the waves of COVID-19 pandemics – A call for a multiobjective compromise. Trends in Anaesthesia and Critical Care, 38, 13-15.

Chagla, Z. (2021). The BNT162b2 (BioNTech/Pfizer) vaccine had 95% efficacy against COVID-19 ≥7 days after the 2nd dose. Annals of internal medicine, 174, JC15.

Ciminelli, G., Garcia-Mandicó, S. (2020). COVID-19 in Italy: An Analysis of Death Registry Data. Journal of Public Health (United Kingdom), 42, 723-730.

Craxi, L., Casuccio, A., Amodio, E., Restivo, V. (2021). Who should get COVID-19 vaccine first? A survey to evaluate hospital workers’ opinion. Vaccines, 9, 1-12.

Creech, C.B., Walker, S.C., Samuels, R.J. (2021). SARS-CoV-2 Vaccines. JAMA - Journal of the American Medical Association, 325, 1318-1320.

Dan, X.M., Zhang, T.W., Li, Y.W., Li, A.X. (2013). Immune responses and immune-related gene expression profile in orange-spotted grouper after immunization with Cryptocaryon irritans vaccine. Fish &amp; shellfish immunology, 34, 885-891.

De Bernardis, F., Amacker, M., Arancia, S., Sandini, S., Gremion, C., Zurbriggen, R., Moser, C., Cassone, A. (2012). A virosomal vaccine against candidal vaginitis: Immunogenicity, efficacy and safety profile in animal models. Vaccine, 30, 4490-4498.

European Centre for Disease Prevention and Control (2021). https://www.ecdc.europa.eu/en/publications-data/data-covid-19-vaccination-eu-eea. Last accessed on 16-Jun-2021: ECDC.
Faranda, D., Alberti, T., Arutkin, M., Lembo, V., Lucarini, V. (2021). Interrupting vaccination policies can greatly spread SARS-CoV-2 and enhance mortality from COVID-19 disease: The AstraZeneca case for France and Italy. Chaos, 31, 1ENG.

Fergie, J., Srivastava, A. (2021). Immunity to SARS-CoV-2: Lessons Learned. Frontiers in Immunology, 12.

Giubilini, A., Savulescu, J., Wilkinson, D. (2021). Queue questions: Ethics of COVID-19 vaccine prioritization. Bioethics, 35, 348-355.

Gobbi, F., Buonfrate, D., Moro, L., Rodari, P., Piubelli, C., Caldner, S., Riccetti, S., Sinigaglia, A., Barzon, L. (2021). Antibody response to the bnt162b2 mrna covid-19 vaccine in subjects with prior sars-cov-2 infection. Viruses, 13.

Grubeck-Loebenstein, B. (1997). Changes in the aging immune system. Biologicals, 25, 205-208.

Hall, V.J., Foulkes, S., Saei, A., Andrews, N., Oguti, B., Charlett, A., Wellington, E., Stowe, J., Gillson, N., Atti, A., Islam, J., Karagiannis, I., Munro, K., Khawam, J., Chand, M.A., Brown, C.S., Ramsay, M., Lopez-Bernal, J., Hopkins, S., Andrews, N., Atti, A., Aziz, H., Brooks, T., Brown, C.S., Camero, D., Carr, C., Chand, M.A., Charlett, A., Crawford, H., Cole, M., Conneely, J., D’Arcangelo, S., Ellis, J., Evans, S., Foulkes, S., Gillson, N., Gopal, R., Goplen, B., Hall, L., Hall, V.J., Harrington, P., Hopkins, S., Hewson, J., Hoschler, K., Ironmonger, D., Islam, J., Kall, M., Karagiannis, I., Kay, O., Khawam, J., King, E., Kirwan, P., Kyffin, R., Lackenby, A., Lattimore, M., Linley, E., Lopez-Bernal, J., Mabey, L., McGregor, R., Miah, S., Monk, E.J.M., Munro, K., Naheed, Z., Nisss, A., O’Connell, A.M., Oguti, B., Okafor, H., Organ, S., Osbourne, J., Otter, A., Patel, M., Platt, S., Pople, D., Potts, K., Ramsay, M., Robotham, J., Rokadiya, S., Rowe, C., Saei, A., Sebbage, G., Semper, A., Shrotri, M., Simmons, R., Soriano, A., Staves, P., Taylor, S., Taylor, A., Tengbe, A., Tonge, S., Vusirikala, A., Wallace, S., Wellington, E., Zambon, M., Corrigan, D., Sartaj, M., Crome, L., Campbell, S., Braithwaite, K., Price, L., Haahr, L., Stewart, S., Lacey, E.D., Partridge, L., Stevens, G., Ellis, Y., Hodson, H., Norman, C., Larru, B., McWilliam, S., Roynon, A., Northfield, J., Winchester, S., Ciciriwa, P., Pai, A., Bakker, P., Loughrey, C., Watt, A., Adair, F., Hawkins, A., Grant, A., Temple-Purcell, R., Howard, J., Slawson, N., Subudhi, C., Davies, S., Bexley, A., Penn, R., Wong, N., Boyd, G., Rajgopal, A., Arenas-Pinto, A., Matthews, R., Whileman, A., Laugharne, R., Ledger, J., Barnes, T., Jones, C., Osuji, N., Chitalia, N., Bailey, T., Akhtar, S., Harrison, G., Horne, R., Walker, N., Agwu, K., Maxwell, V., Graves, J., Williams, S., O’Kelli, A., Ridley, P., Cowley, A., Johnstone, H., Swift, P., Democratis, J., Meda, M., Brake, S., Gunn, J., Selassi, A., Hams, S., Irvine, V., Chandrasekaran, B., Forsyth, C., Radmore, J., Thomas, C., Brown, K., Roberts, S., Burns, P., Gajee, K., Lewis, T., Byrne, T.M., Sanderson, F., Knight, S., Macnaughton, E., Burton, B.J.L., Smith, H., Chaudhuri, R., Aeron-Thomas, J., Hollinshead, K., Shorten, R.J., Swan, A., Favager, C., Murira, J., Baillon, S., Hamer, S., Shah, A., Russell, J., Brennan, D., Dave, A., Chawla, A., Westwell, F., Adeboyeku, D., Papineni, P., Pegg, C., Williams, M., Ahmad, S., Horsley, A., Gabriel, C., Pagget, K., Maloney, G., Ashcroft, J., Del Rosario, P., Crosby-Nwaobi, R., Flanagan, D., Dhasmana, D., Fowler, S., Cameron, E., Prentice, L., Sinclair, C., Bateman, V., McLennand-Brooks, K., Ho, A., Murphy, M., Coochrane, A., Gibson, A., Black, K., Tempest, K., Donaldson, S., Coke, L., Elumogo, N., Elliott, J., Padgett, D., Cross, A., Mirfenderesky, M., Joyce, S., Sinanovic, I., Howard, M., Cowling, P., Brazil, M., Hanna, E., Abdelrazik, A., Brand, S., Sheridan, E.A., Wadams, B., Lloyd, A., Mouland, J., Giles, J., Pottering, G., Coles, H., Joseph, M., Lee, M., Orr, S., Chenoweth, H., Browne, D., Auckland, C., Lear, R., Mahungu, T., Rodger, A., Warren, S., Brookeing, D., Pai, S., Druyeh, R., Smith, E., Stone, S., Meinsner, S., Delgado, D., Underhill, E., Keen, L., Aga, M., Domingos, P., Gormley, S., Kerrison, C., Birch, S., DeSilva, T., Allsop, L., Ambalkar, S., Beekes, M., Jose, S., Tomlinson, J., Painter, S., Price, C., Pepperell, J., James, K., Trinick, T., Moore, L., Day, J., Boulos, A., Knox, I., Defever, E., McCracken, D., Gray, K., Houston, A., Planche, T., Pritchard Jones, R.
Batra, R., Martinez-Nunez, R., Shankar-Hari, M., Edgeworth, J.D., Neil, S.J.D., Malim, M.H., Doores, K.J. (2020). Longitudinal observation and decline of neutralizing antibody responses in the three months following SARS-CoV-2 infection in humans. Nature Microbiology, 5, 1598-1607.

Tenforde, M.W., Olson, S.M., Self, W.H., Talbot, H.K., Lindsell, C.J., Steingrub, J.S., Shapiro, N.I., Ginde, A.A., Douin, D.J., Prekker, M.E., Brown, S.M., Peltan, I.D., Gong, M.N., Mohamed, A., Khan, A., Exline, M.C., Files, D.C., Gibbs, K.W., Stubblefield, W.B., Casey, J.D., Rice, T.W., Grijalva, C.G., Hager, D.N., Shehu, A., Qadir, N., Chang, S.Y., Wilson, J.G., Gaglani, M., Murthy, K., Calhoun, N., Monto, A.S., Martin, E.T., Malani, A., Zimmerman, R.K., Silveira, F.P., Middleton, D.B., Zhu, Y., Wyatt, D., Stephenson, M., Baughman, A., Womack, K.N., Hart, K.W., Kobayashi, M., Verani, J.R., Patel, M.M. (2021). Effectiveness of Pfizer-BioNTech and Moderna Vaccines Against COVID-19 Among Hospitalized Adults Aged ≥65 Years - United States, January-March 2021. MMWR. Morbidity and mortality weekly report, 70, 674-679.

Tufan, A., Avanoğlu Güler, A., Matucci-Cerinic, M. (2020). Covid-19, immune system response, hyperinflammation and repurposantirheumatic drugs. Turkish Journal of Medical Sciences, 50, 620-632.

Vasileiou, E., Simpson, C.R., Shi, T., Kerr, S., Agrawal, U., Akbari, A., Bedston, S., Beggs, J., Bradley, D., Chuter, A., de Lusignan, S., Docherty, A.B., Ford, D., Hobbs, F.R., Joy, M., Katikireddi, S.V., Marple, J., McCowan, C., McGagh, D., McMenamin, J., Moore, E., Murray, J.L., Pan, J., Ritchie, L., Shah, S.A., Stock, S., Torabi, F., Tsang, R.S., Wood, R., Woolhouse, M., Robertson, C., Sheikh, A. (2021). Interim findings from first-dose mass COVID-19 vaccination roll-out and COVID-19 hospital admissions in Scotland: a national prospective cohort study. The Lancet, 397, 1646-1657.

Williams, J., Degeling, C., McVernon, J., Dawson, A. (2021). How should we conduct pandemic vaccination? Vaccine, 39, 994-999.

Wise, J. (2021). Covid-19: European countries suspend use of Oxford-AstraZeneca vaccine after reports of blood clots. BMJ (Clinical research ed.), 372, n699.