The cost-effectiveness of a COVID-19 vaccine in a Danish context

by

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The cost-effectiveness of a COVID-19 vaccine in a Danish context

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Abstract

Vaccines against COVID-19 are under development. As a scarce resource, the health authorities have to decide how to prioritise the vaccine in the target population.

The aim of this paper is to explore the cost-effectiveness of a COVID-19 vaccine and to analyse how the vaccine price, and the cost of administrating it, influence its cost-effectiveness.

We consider an epidemiological model developed by Statens Serum Institut (SSI) to determine the possible effects of a vaccine in terms of the number of life-years gained and hospital cost saved. The model allows us to differentiate between two populations groups, those above and below 60 years of age, respectively. We used the model to consider four scenarios: 1) vaccination of 1.5 million persons 60 years of age or older, none below that age, 2) vaccination of 1.5 million persons below the age of 60 years, none above that age, 3) vaccination of 900.000 persons below 60 years of age and 1.5 million person 60 years of age or older, and 4) 2.4 million persons below the age of 60 years. The time horizon of the analysis is six months, and the perspective is that of the Danish healthcare sector.

The results show that inclusion of the elderly population 60 years of age or older is more cost-effective than a vaccination strategy targeted a population which is younger than 60 years old only. Furthermore, the results show that an extension of the target group from the elderly population only, to also include the younger population comes with an increasing cost per life-year gained. These findings are independent of the specification of the cost of hospitalization for treating COVID-19 infections and the costs of the vaccine. However, the incremental cost-effectiveness ratio depends on the price of the vaccine, hereunder also the administration costs, and the discount rate used for the estimation of life-years gained from a vaccine.

Key Words Cost-effectiveness analysis, COVID-19 vaccine

JEL Codes I18, C63, D60

Introduction

With more than 1.6 million deaths globally (Johns Hopkins Coronavirus Resource Center[1]), the coronavirus disease 2019 (COVID-19) pandemic has had enormous health and economic consequences worldwide.

Currently, extensive research is ongoing worldwide in the search for an effective vaccine against COVID-19[2]. Several candidates for a vaccine are currently being tested (Jonathan Corum, Sui-Lee Wee and Carl Zimmer, Corona Virus Tracker, The New York Times[3]). As of late December 2020, one vaccine has been approved by the European Commission follow by recommendation from the European Medicines Agency.[4]

With a vaccine, it is expected that the many restrictions on human interactions such as assembly banns, quarantines upon entry into a country, and closure of restaurants and shops, to mention a few, that have come with controlling the disease, can be lifted. That is, a vaccine may have significant impact on economic activity in addition to its primary purpose to avoid deaths and severe incidences of illness due to COVID-19 which can put healthcare systems under pressure. Thus, a vaccine is expected to be of high value to society.

However, the exact value of the vaccine depends on a number of factors which remain uncertain. First, the effectiveness of the vaccine, i.e. the ability of the vaccine to prevent infection with the virus that causes COVID-19, in the vaccinated population. As a minimum, the World Health Organization (WHO) requires a vaccine efficacy of 50%, and preferably a 70% efficacy [1].

Second, the price of the vaccination and the costs of administrating it. That is, the total cost of vaccinating the population should be seen in relation to the costs of for example hospital treatment that are expected to be avoided because of reduced incidences of COVID-19.

Furthermore, the value also depends on the cost of treating severe incidences of COVID-19. That is, effective treatment of COVID-19 actually will reduce the value of a vaccine.

As COVID-19 is new and affects the whole world, it is likely that demand for the vaccine will exceed the supply, in particular in the initial phase of its introduction as has been the case with other protective gears. Hence, we expect to have a scarce resource to allocate, at least initially.

Since healthcare systems are organised nationally, all countries in the world need to handle this shortage of vaccines in the short run. In the long run, national policy makers may also need to consider how the distribution of a vaccine should be organised and how it should be financed.

In this paper we address these questions from the perspective of the Danish healthcare system.

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[1] https://coronavirus.jhu.edu.

[2] https://laegemiddelstyrelsen.dk/da/nyheder/temaer/ny-coronavirus-COVID-19/~/media/3A4B7F16D0924DD8BD157BBE17BFED49.ashx.

[3] https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html.

[4] https://www.ema.europa.eu/en

In Denmark, universal healthcare coverage is provided to all permanent residents by five regions [2]. Each region owns and runs its hospital, whereas primary healthcare is provided by self-employed general practitioners (GPs) by contract with the regions. Each resident is listed with a GP, and GPs are reimbursed by a combination of capitation (based on the number of residents on their list) and fee-for-service [2]. Hospital treatment and healthcare services from GPs are with a few exceptions provided free of charge to patients.

In terms of vaccination, all children in Denmark are covered by a national comprehensive childhood vaccination programme, which among others include vaccination against indiphtheria, tetanus, pertussis (whooping cough), polio (infantile paralysis), measles, mumps, rubella [3]. The human papillomavirus (HPV) vaccination against cervical cancer for girls has been included in the programme since 2009 [4]. Since 2019, HPV vaccination for boys has been included in the programme [5].

In the national programme, all persons aged 65 years of age or older and persons with chronic diseases are recommended to be vaccinated against seasonal influenza and pneumonia, and they can have these vaccines free of charge.

The regions cover the cost of vaccination that are included in the national immunization programmes [2].

The cost-effectiveness of these vaccines has been studied in a Danish context previously, even though such considerations may not have been included directly in the decision to include these vaccinations in the Danish Immunization programme [6-10].

The aim of this paper is to explore the cost-effectiveness of a COVID-19 vaccination. However, since a significant number of aspects of such vaccine remain uncertain, including vaccine efficacy, availability, and target groups for a vaccine, we aim to analyse how these aspects influence the cost-effectiveness of the vaccine though.

A substantial element of the vaccination programme is the amount of vaccines available to the Danish population and the frequency with which these vaccines can be distributed in the society. In the present analysis we assume that a limited dose of vaccines is available for the Danish population. We base our number on a best guess for the demand of such vaccine combined with the previous agreement between the European Union (EU) and the medical industry ensuring that 40% of the population can be vaccinated. In Denmark this will correspond to 2.4 million doses. We define a vaccination dose as a full vaccination of one person independent on the number of vaccinations needed to complete the full vaccination. Whether 2.4 million will be available upfront for the Danish population is uncertain. Furthermore, 40% of the population is a very high vaccination ratio compared to the regular annual vaccination against seasonal influenza where between 10%-15% of the Danish population on an annual basis have had the vaccine in the period from 2009-2019 [10]. In 2020, more that 1.1 million Danes have been vaccinated against seasonal influenza, corresponding to about 20% of the population.[5] We, therefore, present two different scenarios with 1.5 million and 2.4 million doses, respectively.[6]

For the purpose of finding the best allocative efficiency different alternatives implementing a COVID-19 vaccine are defined. For these alternative interventions the incremental cost-effectiveness ratios from implementing a vaccination programme are determined. At the state of preparing the analysis the vaccine against COVID-19 is not yet available. The analysis looks into different strategies for whom to vaccinate. Also, the availability of the vaccine is unknown. The alternatives are defined based on past experience with vaccination programmes combined with the structure of the impact model. Based on the alternative interventions defined, policy recommendation towards which vaccination programme to pursue is provided.

Methods

We designed this study as a cost-effectiveness analysis in which we calculated the incremental cost-effectiveness ratio (ICER). The ICER was calculated as the difference in costs between two alternatives relative to differences in the effects of the alternatives, $ICER = \frac{\Delta C}{\Delta E} = \frac{C_1 - C_2}{E_1 - E_2}$, where subscript refers to the alternatives, C and E refers to costs and effects, respectively. As we studied several mutually exclusive alternatives, the alternatives were first ordered according to their effects. To calculate the ICER, an alternative was compared to the next best effective alternative.

The differential equation model we consider is developed by an expert group in Statens Serum Institut (SSI) [13], see Figure 1. In contrast to Markov Cohort models (as e.g. used in [23]), this is a continuous time model.

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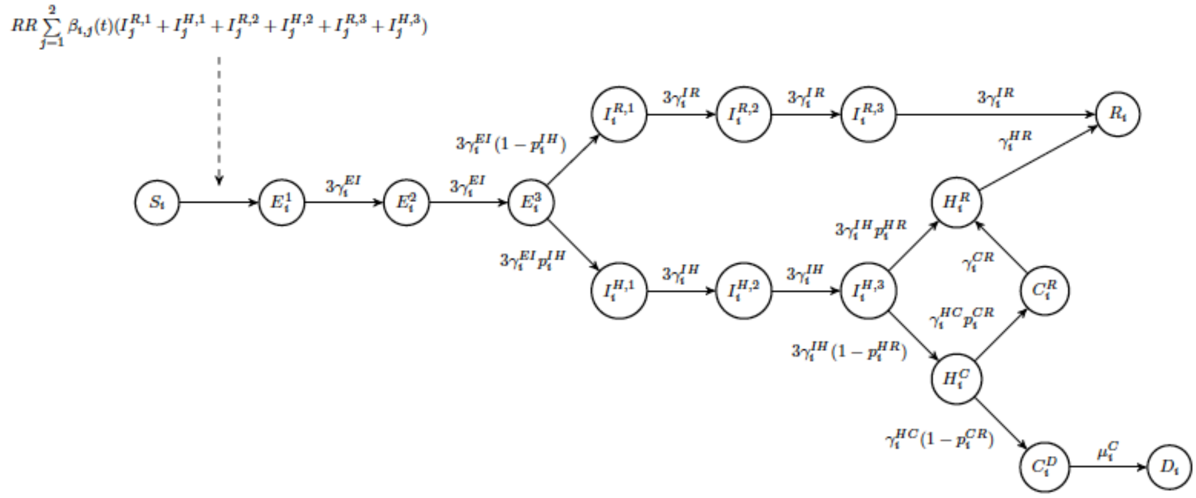
[5] https://www.dr.dk/nyheder/indland/ssi-aabner-noedlagret-paa-omkring-100000-influenzavacciner.

[6] Our scenarios are defined as number of people being vaccinated. With the current approved vaccines each person requires two doses to obtain immunity. At the time of writing the availability of the vaccines is uncertain. The scenarios can be interpretated as the number of persons who are willing to take the vaccines and who obtains full immunity, thus the scenarios also should include capture that some people may decline the vaccination. The scenarios can be adjusted.

Figure 1. SSI's extended structured SEIR model.



Here, S denotes the percentage of individuals susceptible to the virus, E^1 to E^3 the percentage of individuals having been exposed, so being infected but not yet infecting themselves, $I^{R,1}$ to $I^{R,3}$ percentage of infected individuals recovering at home, $I^{H,1}$ to $I^{H,3}$ percentage of infected individuals that will need hospital care, H^R percentage of hospitalized individuals recovering, H^C percentage of hospitalized individuals coming in need for intensive care, C^R percentage of individuals on intensive care that are going to recover, C^D percentage of individuals on intensive care that are going to die, D the percentage of individuals that died in the hospital. Each state distinguished between patients at least sixty years old ($i=2$) and patients younger than 60 years ($i=1$).

For details about parameter ranges and the associated ordinary differential equation model see [12,13]. As described there, we do repeated simulations (bootstraps, in our case 10.000) with parameters chosen uniformly from the given parameter ranges. These simulations are then weighted according to how good the number of hospitalized individuals predicted fit the actual number of hospitalized individuals in Denmark between March 11th and August 26th. The 60% of simulations that fit worst are discarded. For the convenience of the reader, the differential equation model is also listed in Figure 2, and we list parameters and initial values used in the Appendix. We implemented the differential equation model in MATLAB and solved it using the stiff solver *ode15s* [11].

As this model predicts the number of individuals dying on intensive care due to COVID-19, while the official definition of COVID19-related deaths counts the individuals dying within 30 days after a COVID-19 diagnosis, we determined the ratio between the cumulative number of individuals on intensive care and number of individuals dying within 30 days after a COVID-19-diagnosis from March 11th to August 26th, and used this ratio in our simulations to estimate the number of individuals dying from COVID-19 from the cumulative number of individuals needing intensive care.

Figure 2. Differential equations associated to the SEIR model.

$$\frac{d}{dt}S_\iota = -S_\iota\beta_{\iota,\cdot}(t)\cdot(I^{R,1}+I^{H,1}+I^{R,2}+I^{H,2}+I^{R,3}+I^{H,3})RR$$

$$\frac{d}{dt}E_\iota^1 = S_\iota\beta_{\iota,\cdot}(t)\cdot(I^{R,1}+I^{H,1}+I^{R,2}+I^{H,2}+I^{R,3}+I^{H,3})RR-3\gamma_\iota^{EI}E_\iota^1$$

$$\frac{d}{dt}E_\iota^2 = 3\gamma_\iota^{EI}E_\iota^1-3\gamma_\iota^{EI}E_\iota^2$$

$$\frac{d}{dt}E_\iota^3 = 3\gamma_\iota^{EI}E_\iota^2-3\gamma_\iota^{EI}E_\iota^3$$

$$\frac{d}{dt}I_\iota^{R,1} = 3\gamma_\iota^{EI}E_\iota^3(1-p_\iota^{IH})-3\gamma_\iota^{IR}I_\iota^{R,1}$$

$$\frac{d}{dt}I_\iota^{H,1} = 3\gamma_\iota^{EI}E_\iota^3p_\iota^{IH}-3\gamma_\iota^{IH}I_\iota^{H,1}$$

$$\frac{d}{dt}I_\iota^{R,2} = 3\gamma_\iota^{IR}I_\iota^{R,1}-3\gamma_\iota^{IR}I_\iota^{R,2}$$

$$\frac{d}{dt}I_\iota^{R,3} = 3\gamma_\iota^{IR}I_\iota^{R,2}-3\gamma_\iota^{IR}I_\iota^{R,3}$$

$$\frac{d}{dt}I_\iota^{H,2} = 3\gamma_\iota^{IH}I_\iota^{H,1}-3\gamma_\iota^{IH}I_\iota^{H,2}$$

$$\frac{d}{dt}I_\iota^{H,3} = 3\gamma_\iota^{IH}I_\iota^{H,2}-3\gamma_\iota^{IH}I_\iota^{H,3}$$

$$\frac{d}{dt}H_\iota^R = 3\gamma_\iota^{IH}I_\iota^{H,3}p_\iota^{HR}+\gamma_\iota^{CR}C_\iota^R-\gamma_\iota^{HR}H_\iota^R$$

$$\frac{d}{dt}H_\iota^C = 3\gamma_\iota^{IH}I_\iota^{H,3}(1-p_\iota^{HR})-\gamma_\iota^{HC}H_\iota^C$$

$$\frac{d}{dt}C_\iota^R = \gamma_\iota^{HC}H_\iota^Cp_\iota^{CR}-\gamma_\iota^{CR}C_\iota^R$$

$$\frac{d}{dt}C_\iota^D = \gamma_\iota^{HC}H_\iota^C(1-p_\iota^{CR})-\mu_\iota^CC_\iota^D$$

$$\frac{d}{dt}R_\iota = 3\gamma_\iota^{IR}I_\iota^{R,3}+\gamma_\iota^{HR}H_\iota^R$$

$$\frac{d}{dt}D_\iota = \mu_\iota^CC_\iota^D$$

$$\frac{d}{dt}HCum_\iota = 3\gamma_\iota^{IH}I_\iota^{H,3}$$

$$\frac{d}{dt}CCum_\iota = \gamma_\iota^{HC}H_\iota^C$$

The time-horizon of our analysis was a 6-months period. It may seem like a short time horizon, but the uncertainties about the development and mutations of the virus are significant, and comparing with alternative similar vaccinations, like for instance a vaccination against the flu, these last for a shorter time horizon and have to be renewed on an annual basis.

In the model we used gained life year (LY) as the measure of effectiveness. The LY allowed us to determine the efficiency of the different alternatives since it adjusted the number of lost lives with the age of the patient. We found the cumulative effects over a 6-month period, which we defined from the beginning of the COVID-19 pandemic, hence our numbers were simulated based on the period from March 2020 until and including august 2020. We determined the total additional effects of the intervention which was the saved life years with vaccination compared to the situation with no vaccination. Also, we determined the total additional costs saved comparing the intervention with vaccination with a situation without vaccination. The costs were composed of change in hospitalization costs (expected to decrease after the intervention).

The epidemiologic model allowed us to differentiate between two groups of individuals, those above and below 60 years of age, respectively. Combining this with the doses available we defined the following scenarios to be evaluated. We used the following notation in our description of the different scenarios. $Vaccinated\, population = (v; w)$ refers to that v numbers of people in the group of people of the population below 60 years old was vaccinated and w numbers of people in the group of people of the population above and including 60 years old was vaccinated. We measure v and w in million people. Based on the Danish statistics the number of persons 60 years old or older was in the 3rd quarter 2020 1,513,240 people. We proxy this by 1.5 million [14].

In the model we present four different scenarios and compare them to the status quo where no-one is vaccinated. Hence in status quo the $Vaccinated\, population = (0; 0)$. The other scenarios depend on the availability of the vaccine. We define four mutually exclusive scenarios where two of these scenarios assume an availability of 1.5 million doses of vaccine distributed as

1. Only population above and including 60 years old (≥ 60) is vaccinated.
   $Vaccinated\, population = (0; 1.5)$
2. Only population below 60 years old (< 60) is vaccinated.
   $Vaccinated\, population = (1.5; 0)$

The other two scenarios assume an availability of 2.4 million doses distributed as

3. Population above and including 60 years old (≥ 60) is first prioritized for vaccination, the remainder of the doses are used in the population below 60 years old (< 60).
   $Vaccinated\, population = (0.9; 1.5)$
4. Only population below 60 years old (<60) is vaccinated.
   $Vaccinated\, population = (2.4; 0)$

For modelling purposes, we assume that the doses are available from the beginning of the time period applied in the model.

Resource use and costs

All costs were measured for the year 2020 and reported in Danish kroner (DKK).[7] The perspective of the analysis was that of the national healthcare service in Denmark, and the model was designed to estimate the healthcare costs of various scenarios for the administration of a vaccine.

The costs included those of the purchase and administration of the vaccine, the costs of hospitalization of patients because of an infection with COVID-19 virus, the costs of testing for corona virus, and cost to general practitioners for their follow-up service on a detection of a virus infection. We define this as healthcare costs in our study. Costs such as late complications of a COVID-19 infection or absenteeism from work were not incorporated in the analysis.

The cost of vaccination incorporates a number of uncertainties. First, apparently the price of the vaccine varies widely. Second, the cost of administering the vaccine will depend on the organisation of the vaccination programme. To deal with these uncertainties, we varied the unit cost from 300 to 500 DKK per vaccinated person, where we assumed that each person requires two vaccinations to be fully immunized against COVID-19. We based this on the following reason.

First, based on a now deleted entry on a social media platform by a European minister of health, news media reported the price of the vaccines to be in the interval from 13 to 109 DKK per dose.[8]

Second, since some of the vaccinations in Denmark will be carried out by general practitioners, the regional health authorities have made an agreement with the general practitioners' organization. In this agreement, a general practitioner is remunerated with 146.25 DKK for a vaccination that is given on weekdays between 8 and 16 o'clock, whereas vaccination in the evening and weekends will be remunerated with 202.78 DKK or 251.75 DKK.[9] We expected that most vaccinations will be carried out during weekdays within normal working hours. Furthermore, it is expected that general practitioners primarily vaccinate persons who live in nursing homes, whereas vaccinations of the rest of the Danish population is expected to take place in vaccination centres, which are to be set up by the Danish Regions.[10]

The cost of hospitalization was estimated on the basis of the diagnosis related group (DRG) tariffs, which reflect the average cost for treatment in Danish publicly owned hospitals [15]. Furthermore, it was based on documentation by The Danish Health Data Authority (DHDA; Sundhedsdatastyrelsen, in Danish) on how to assign hospitalizations due to COVID-19 in the DRG system [16]. Unfortunately, we were not able to access information on the distribution of hospitalized patients on their diagnoses and DRG classification.

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[7] 1 USD corresponds approximately to 6 DKK, 1 EUR corresponds approximately 7.4 DKK (January, 2021).

[8] TV2, Minister kom til at afsløre hemmelig prisliste - så meget koster de forskellige vacciner, 19th December 2020, https://nyheder.tv2.dk/udland/2020-12-19-minister-kom-til-at-afsloere-hemmelig-prisliste-saa-meget-koster-de-forskellige (last accessed 8th January 2021).

[9] Praktiserende Lægers Organisation, COVID-19-vaccine, https://www.laeger.dk/PLO/covid-19-vaccine#honorar (last accessed 8th January 2021).

[10] Sundhedsstyrelsen, Selve vaccinationsprogrammet, https://www.sst.dk/da/corona/Vaccination-mod-COVID-19/Selve-vaccinationsprogrammet (last accessed 8th January 2021).

We assumed that patients were hospitalized for more than one day, and that patients who were hospitalized in an intensive care unit suffered from a severe acute respiratory syndrome (DHDA classification code DB972A), whereas patients who were hospitalized outside an intensive care unit suffered from COVID-19 infection without specification of the localization (DHDA classification code DB342A), and that patients hospitalized outside an intensive care unit did not suffer from complications. We also assumed that all hospitalized patients were 18 years old or older. The latter was based on the observation that less than three percent of all hospitalized patients were 19 years old or younger.[11] The DRG code and tariff differed by age groups for patients with severe acute respiratory syndrome.

In accordance with the DHDA's classification, patients that were in respirator treatment were assumed to be classified in one of four groups of intensive care, which included organ failure.

Since the distribution of patient diagnoses and DRG classifications were unknown, we used three different specifications for the hospitalization cost parameters.

The unit costs for these three specifications are presented in Table 1. In particular, the unit cost for patients in respirator treatment varied.

In the presentation of the results, we used specification number 1 as the base case, and used the other specifications for sensitivity analyses to examine how the cost-effectiveness of a vaccine would be affected in changes in the assumptions about hospitalization costs.

Finally, we expected that a vaccine would reduce the number of tests for infection with the virus which causes COVID-19. We assumed that the unit cost of a test was 200 DKK based on information from the regional health authorities interest organization Danish Region brought forward in news media. The unit costs included test equipment, reagents, and salary to staff who carry out the test and the analyses of the test.[12]

In addition to the cost of the test, we included the costs to general practitioners' follow-up services on the detection of virus in a test. According to the agreement between the Danish regional health authorities and the general practitioners' organisation, the general practitioners are remunerated with 146.25 DKK.[13]

To carry out the analyses we needed an estimate of the number of people diagnosed with COVID-19 and we need an estimate of the number of tests.

The number of people being diagnosed with COVID-19 required a stepwise calculation as the epidemiological model only calculated the number of people being infected. To transform the cumulative number of individuals infected with COVID-19 to the number of people being diagnosed we needed to know the proportionality between the two. Thus, we calculated the ratio of the estimated weighted median of the cumulative number of infected individuals, when no vaccine was provided, to the actual number of individuals diagnosed with COVID-

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[11] Statens Serum Institut, Indlagte patienter: køn og alder - akkumuleret https://www.sst.dk/da/corona/status-for-epidemien/tal-og-overvaagning#2 (last accessed 18th December 2020).

[12] BT, Så meget koster det regionerne at teste én person for corona, 18th September 2020 (last accessed 8th January 2021).

[13] https://www.sundhed.dk/sundhedsfaglig/information-til-praksis/syddanmark/almen-praksis/nyheder-og-meddelelser/nyhedsbreve/nyt-fra-regionen/nyt-2020-juni-test-henvisning-naere-kontakter/ (last accessed 20th January 2021).

19 until August 26th, 2020 in Denmark. This ratio allowed us to estimate the number of people being diagnosed.

To estimate the number of tests, we used the proportion of the total number of tests that were carried out as of 26th August 2020 relative to the cumulative number of persons diagnosed with COVID-19 as of this date. Then, this proportionality factor was multiplied with the estimated number of people being diagnosed in our model.

Table 1. Three specifications of the unit costs for hospitalization. Danish kroner (DKK)

Specification 1	DRG code	Unit cost (DKK)
Hospitalization outside intensive care unit, patients 18 years old or older	18MA06	16,495
Hospitalization in an intensive care unit		
Patients 18-59 years old	04MA14	26,028
Patients 60 years old or older	04MA13	37,050
Hospitalization in respirator	26MP11	255,171
Specification 2	**DRG code**	**Unit cost (DKK)**
Hospitalization outside intensive care unit, patients 18 years old or older	18MA06	16,495
Hospitalization in an intensive care unit		
Patients 18-59 years old	04MA14	26,028
Patients 60 years old or older	04MA13	37,050
Hospitalization in respirator	26MP09	479,862
Specification 3	**DRG code**	**Unit cost (DKK)**
Hospitalization outside intensive care unit, patients 18 years old or older	18MA06	16,495
Hospitalization in an intensive care unit		
Patients 18-59 years old	04MA14	26,028
Patients 60 years old or older	04MA13	37,050
Hospitalization in respirator	04MA13	37,050

Source: Sundhedsdatastyrelsen, DRG-takster 2020 [15].

Life-years

The model used life-years to study the health effects of a vaccine against COVID-19. For this purpose, we estimated the number of lost life years for individuals dying younger or older than 60 years, we weighted the expected number of life years for men and women in the age groups 20-59,60-69, 70-79, 80-89 and 90-99 retrieved from Statistics Denmark [17-18] with the relative occurrence of men and women in those age groups among the individuals infected with COVID-19 that according to SSI had died until June 3rd, 2020 at 14.20 [19].

Life-years gained are presented undiscounted and discounted with a discount rate of 2% or 4% (Table 2), as the Ministry of Finance recommends a discount rate of 4% for projects with a time horizon up to 35 years and 2% for effects beyond 35 years [20].

Table 2. Life-expectancy by age group.

Age group	Life-expectancy, years		
	Un-discounted	Disc. Rate = 2%	Disc. Rate = 4%
20-59 years old	41.9	28.7	21.0
60+ years old	8.9	8.0	7.3
Note: Estimated on the basis of data from Statistics Denmark [17-18], and weighted by the age distribution of those who died [19].			

Assumptions

In the model simulation we assume that the vaccination provides 100% effectiveness, hence the vaccinated population is completely immune towards COVID-19. We assume that the vaccine gives immunity for the duration of six months. Recent research shows a vaccine effectiveness up to about 95% [21]. The presented results in the forthcoming section are therefore presenting the more positive outcome of a vaccination programme.

The epidemiological model is calibrated to the observations in the spring 2020 and not the autumn 2020, it therefore implicitly assumes that the human behaviour related to social distance, facemasks in public transportation, hygiene, cleaning as of spring 2020 is maintained.

Results

The following sections shows the results from the simulation model. Table 3 shows the number of life-years lost under the five alternatives and based on the number of life-years gained from a vaccination programme to various target groups. From this analysis we see that vaccination programmes that included the elderly population 60 years of age or older increased the number of life-years gained compared to programmes targeted those below 60 years of age only.

Table 3. Estimated life-years gained by the four vaccination scenarios.

Scenario	Lost life year (years, undiscounted)		Life-years gained (Q50)		
	Q50	Q25-Q75	Disc.rate 0%	Disc.rate 2%	Disc.rate 4%
Status quo: (0;0)	10,930	7,579-16,001			
1: (0;1.5)	6,462	4,559-9,452	4,468	3,834	3,379
2: (1.5;0)	7,342	5,519-9,532	3,588	2,917	2,399
3: (0.9;1.5)	5,341	3,842-7,366	5,589	4,690	4,049
4: (2.4;0)	6,446	4,896-8,292	4,484	3,580	2,963

Q50 is the weighted median. It extends the standard median taking into account the varying agreement of the predicted and actual numbers of individuals hospitalized in Denmark between March 11th and August 26th, 2020. Q25-Q75 is the interquartile range.

Table 4. Healthcare costs by vaccination scenario including test and follow up and hospital cost specification. 1000 DKK.

Scenario	Specification			
	1		2*	3*
	Q50	Q25-Q75	Q50	Q50
Status quo: (0;0)	584,319	442,028-852,206	646,757	522,016
1: (0;1.5)	446,520	361,316-595,135	479,596	415,666
2: (1.5;0)	383,741	333,405-445,531	430,717	339,387
3: (0.9;1.5)	353,894	307,141-411,798	382,645	325,951
4: (2.4;0)	328,928	294,052-369,095	370,285	287,967

Note: *Interquartile range not included; available upon request to the authors.

Table 4 shows the healthcare costs under the five alternatives and with the three different specifications of the cost parameters for hospital in the model. It shows that healthcare costs were lower with a vaccination programme than without vaccination.

The cost of hospitalization accounts for between 14-23% of the total healthcare costs in specification 1. It is slightly more in specification 2 and slightly less in specification 3. As healthcare costs are composed of hospital costs, and costs of testing and follow up, it follows directly that the healthcare costs will be reduced the more people being vaccinated. It is important to notice that, as the hospital costs only account for a smaller share of the healthcare costs, the lower infection rate in a population group also implies less testing and follow up costs.

Figure 3 presents the cost-effectiveness plane applying specification 1 for the hospital costs with undiscounted life-years. The reader can find similar graphs for respectively 2% and 4% discounting of gained life years in Appendix B.

From reading Figure 3 it becomes apparent that in most cases both scenarios 2 (1.5;0) and 4 (2.4;0), which only target the population below 60 years of age, would be dominated by alternatives that include the elderly population in the target group. In our analysis, this is true in all cases expect for scenario 2 with undiscounted life years and when the total price of vaccination is sufficiently low, e.g. 300 DKK.

Figure 3. Cost-effectiveness plane for hospital cost specification 1 and 0% discounting of Life Years gained.

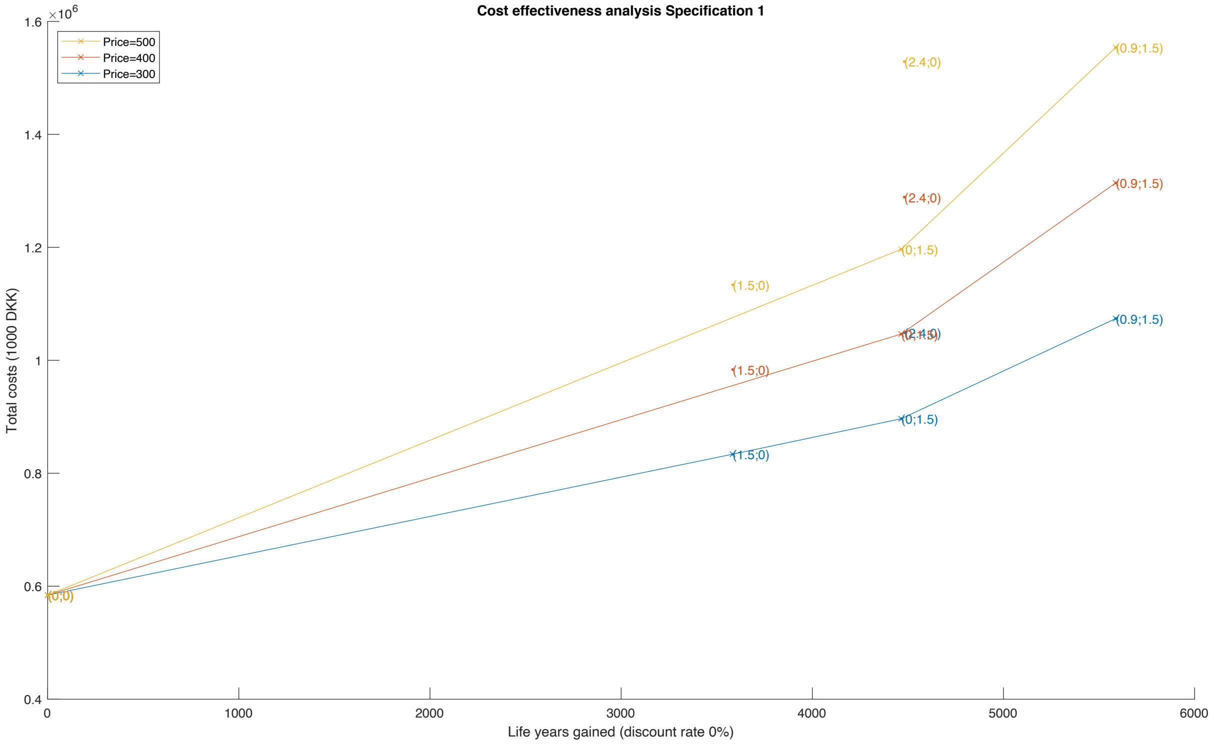
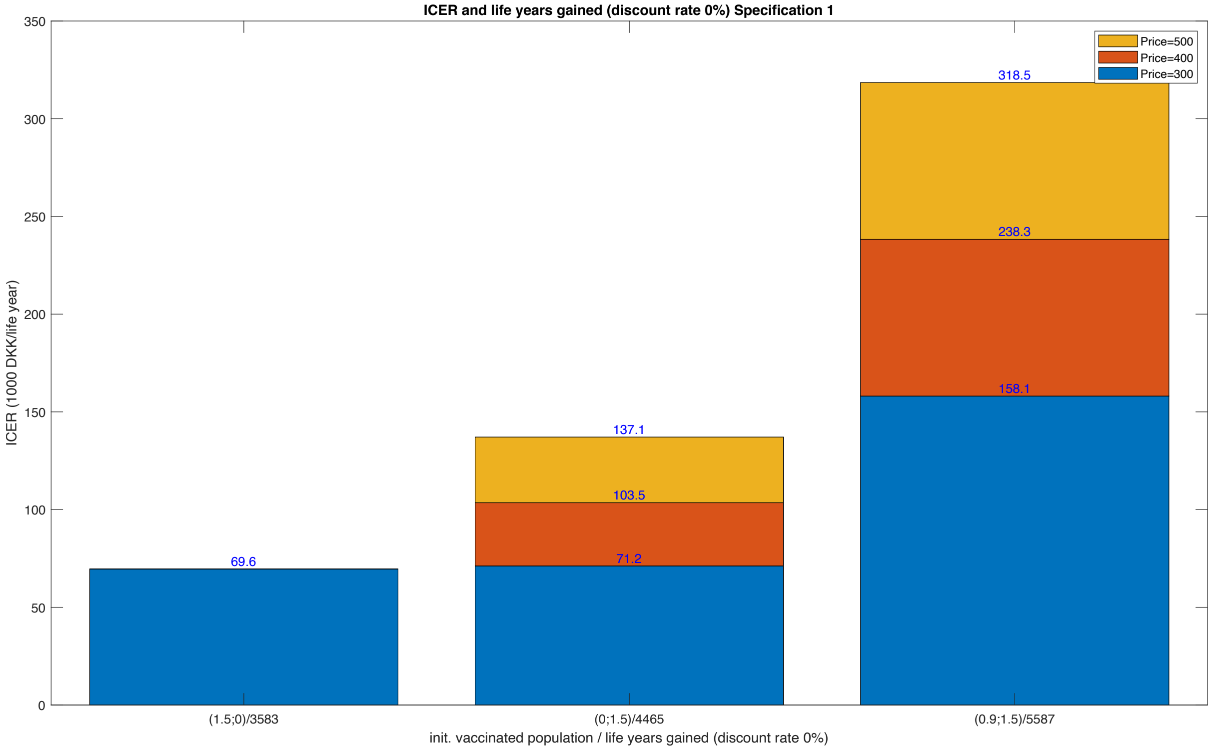


Figure 3 shows the cost-effectiveness plane for the four vaccination programmes and the status quo alternative without vaccination. In the figure the costs of the vaccination were included with various specifications in the range from 300 DKK to 500 DKK per dose. The colour of the points refers to the cost of the vaccination. For each vaccination cost specification, the frontier is represented with the linear connections between the alternatives with the lowest costs and the highest number of life-years gained. Points above the frontier are dominated by alternatives on the frontier.

Figure 4 illustrates the incremental cost-effectiveness ration for the vaccinations programmes not dominated for the six various specification in the range from 300 DKK to 500 DKK per dose. The figure includes the gained life-years undiscounted and discounted with a discount rate of 2% or 4%.

Figure 4 illustrates the effect on the ICER with different price specifications. The ICER is significant lower for the scenario of 1.5 million doses compared to the scenario of 2.4 million doses of vaccine. The figure also illustrates the marginal increase in the ICER with discounting of gained life years. Furthermore, the figure also illustrates that in scenario 2, with undiscounted life years, this programme cannot be excluded. It demonstrates the lowest ICER and hence indicates that it could in some cases be cost-effective to vaccinate the population below 60 year before the population above 60 years old. The figures with 2 and 4% discounting of gained life years are available in Appendix C.

Figure 4. Incremental cost-effectiveness ratio for different costs of the vaccination and for gained life years (undiscounted)



Robustness check

Due to the uncertainty about the distribution of hospitalized patients on their diagnoses and DRG classification we do a robustness check of our results using the costs as described in Table 5.

Table 5. Incremental cost-effectiveness ratio for different cost specifications of hospitalization in 1,000 DKK.

Disc. rate	Scenario	Specification 1	Specification 2	Specification 3
0%	(1.5;0)	70[a]	-	75[a]
	(0;1.5)	71-137	63 - 131	87 - 144
	(0.9;1.5)	158-319	154 - 315	161- 321
2%	(0;1.5)	81-160	74 - 152	90 - 168
	(0.9;1.5)	208- 418	202 - 413	211 - 421
4%	(0;1.5)	92 - 181	84 - 172	102 - 190
	(0.9;1.5)	266 - 536	259 - 529	270 - 540

Note: The intervals describe the ranges for the vaccination price including administration costs in the interval 300 -500 DKK. [a] indicates that only for P=300 the scenario is included.

From Table 5 we conclude that the incremental cost-effectiveness ratio for a gained life year given the intervention with a vaccination programme is not very sensitive to the costs of hospitalization.

We have presented and defined four scenarios with up till 2.4 m people being vaccinated. At the time of writing, it is uncertain how many doses of vaccine that will be available and when they will be available. For the sake of comparison, we have also examined a scenario where 70% of the total Danish population is vaccinated. This scenario would imply vaccination of 3.01 million people in the age group below 60 years old and 1.26 million people in the age group above 60 years old. The gain in life years would be 6,483 (undiscounted) which should be compared with the numbers in Table 3.

If on the other hand, this 70% scenario is compared to doing nothing, the incremental cost effectiveness ratio compared to status quo would be in the range from app. 147-279 measured in 1000 DKK with the vaccination prince ranging from 300 to 500.

Discussion

In this study we aimed to examine the cost-effectiveness of a vaccine against COVID-19, where we added an economic component to an epidemiological model. The results show that inclusion of the elderly population 60 years of age or older in most cases is more cost-effective than a vaccination strategy targeted a population which is younger than 60 years old only. Furthermore, the results show that an extension of the target group from the elderly population only to also include younger populations comes with an increasing cost per life-year gained. These findings were independent of the specification of the cost of hospitalization for treating COVID-19 infections and the price of the vaccine. However, the incremental cost-effectiveness ratio depends on the price of the vaccine and the administration costs. Furthermore, the discount rate used for the estimation of life-years gained from a vaccine influences the incremental cost-effectiveness ratio.

The analysis took its outset in an amount of vaccines that could cover 2.4 million persons. Our model presents the cost-effectiveness ratio for the different scenarios which allows for comparison of these ratios in-between scenarios and to other vaccination programmes. In an alternative scenario we examined the cost-effectiveness of a vaccination strategy where 70% of the adult population is vaccinated. The results suggest that the costs per life-year gained are within the same range as those in the four scenarios we analysed initially.

An essential strength of this study is that we build on an epidemiological model for the Danish population. The epidemiological model has been developed by an expert team at Statens Serum Institut [12]. The model simulates the epidemic in Denmark from its onset in the spring 2020 and forward. We added a component to include the possibility of vaccination and costs parameters, primarily the hospitalization costs of treating COVID-19 infections, and an effectiveness measure in terms of life-years gained. The cost-effectiveness analysis is therefore simulated on a scenario like the one in the first six month of the epidemic in Denmark.

However, the results should also be seen in light of a number of limitations. First, detailed information about the costs of hospitalization for treatment of COVID-19 infections are not available at the time of writing. Thus, the analysis is based on assumptions presenting different costs specifications. Furthermore, more detailed information about the healthcare costs of COVID-19 infections would be useful for an update of the model.

In addition, we do not include costs outside the healthcare sector. It is well known that governments impose restrictions such as lock-downs, assembly bans and other measures to limit the spread of the virus, which cause COVID-19. The costs of managing the epidemic are significant [22]. These costs affect the whole society and not only the individuals who are infected.

Also, we do not include productivity losses due to infections. That is, costs due to lower or lost ability to work because of COVID-19 infections. Furthermore, there can also be productivity costs due to quarantine while individuals who suspect they are infected wait for a test.

Because costs outside the healthcare sector and productivity losses are not included, we regard the presented estimates of cost per gained life year as an upper price of the life-years gained in a vaccination programme.

In a study of the economic value of a COVID-19 vaccine in the USA, Kohli et al. finds that a vaccination would be cost-saving in the high-risk group, and that incremental cost-effectiveness ratios below 50,000 US$ per quality-adjusted life-year gained in other risk groups assuming a single dose vaccine cost of 35 US$ (70 US$ per course, i.e., two doses) [23]. This study differs from our study in several ways. First, they use a Markov cohort model with five health states, whereas we use a differential equation model. Second, the time horizon of the study is one year, whereas we us a time horizon of six months. Third, they include that the vaccine efficacy may be less than 100%.

As mentioned in the introduction, a number of vaccines are included in the Danish immunization programme. The cost-effectiveness of these vaccines has been examined in previous studies. The HPV vaccine, which was introduced in 2009 in Denmark, has been shown to cost 85,000-139,000 DKK per life-year gained (2007 values, 3% discount rate) without productivity costs [7], whereas an expansion of that programme to include boys has been found to cost 33,000 DKK per quality-adjusted life-year gained (2019 values) without productivity costs [8].

In analyses of screening programmes against cancer, the incremental cost-effectiveness ratios of these programmes have been found to be in the range of 76,000-157,000 DKK per life-year gained (2008 values) [24].

Compared to these estimates, our findings of the cost per life-year gained for a vaccination against COVID-19 for the elderly population are within the ranges of that for other preventive programmes in Denmark. For the population below 60 years of age, the cost-effectiveness of a vaccine depends on the price of the vaccine including the administration costs. Demonstration of the cost-effectiveness of the vaccine to this age group would require additional analyses including also cost outside the healthcare sector and productivity costs caused by COVID-19.

Conclusion

In conclusion, the elderly population should almost always be part of the target group for a COVID-19 vaccination programme. There are few exceptions if the price of vaccination including administration is sufficiently low and the life years gained are not discounted. In these cases, it could be more cost-effective to vaccinate the young population. If, however, the aim is to achieve the highest number of life years gained given a limited availability of doses of the vaccine, then the older population should receive the vaccination.

Compared to other interventions, e.g., cancer screening programs, COVID-19 vaccination of the elderly population is cost-effective for cost of vaccination. For the population group below 60 years old the cost-effectiveness compared to other programmes depends on the costs of the vaccination and the discount rate and other costs related to COVID-19 not included in our model. The discounting of life years gained affects the costs of life-years gained.

These results are robust to the changes in the assumption of the hospitalization cost for treatment of COVID-19 infections. That is, the incremental cost-effectiveness ratio is largely unaffected by the hospitalization cost specification.

A COVID-19 vaccination is a potential candidate for a cost-effective intervention in the Danish healthcare sector. Further research on the healthcare costs for treatment of COVID-19 and other societal costs due to COVID-19 is recommended for a comprehensive analysis of its cost-effectiveness.

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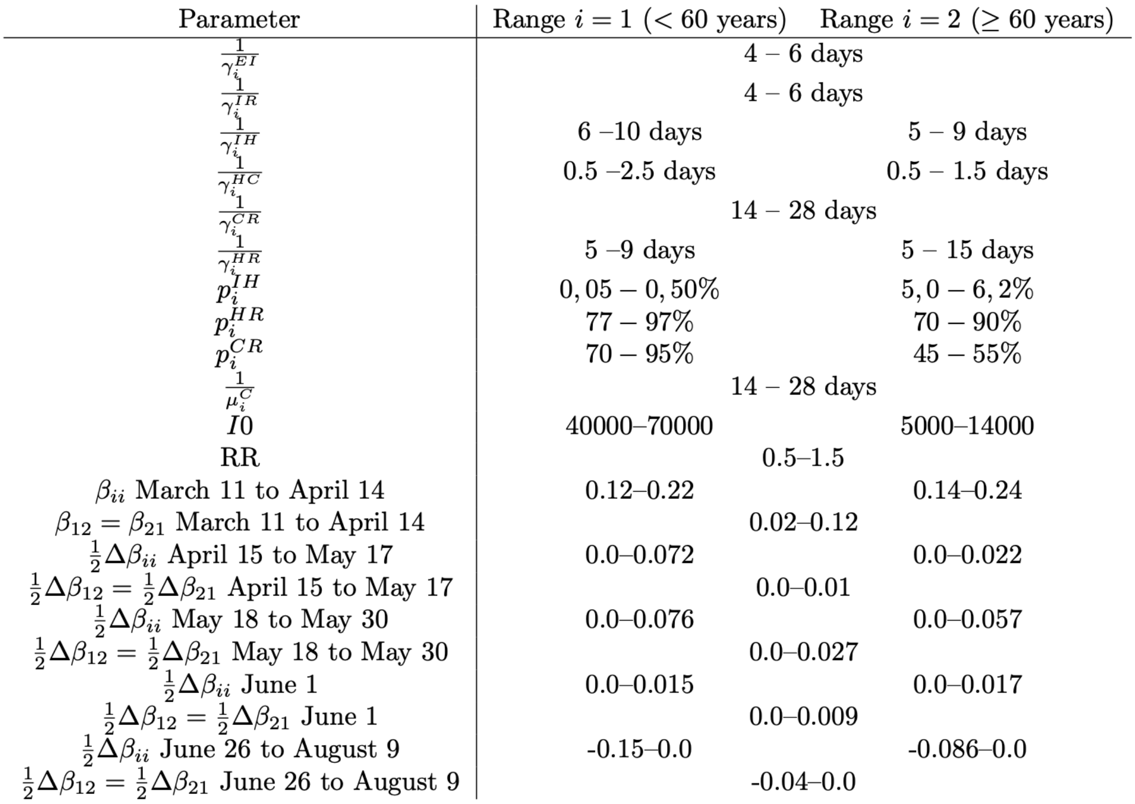
Appendix A

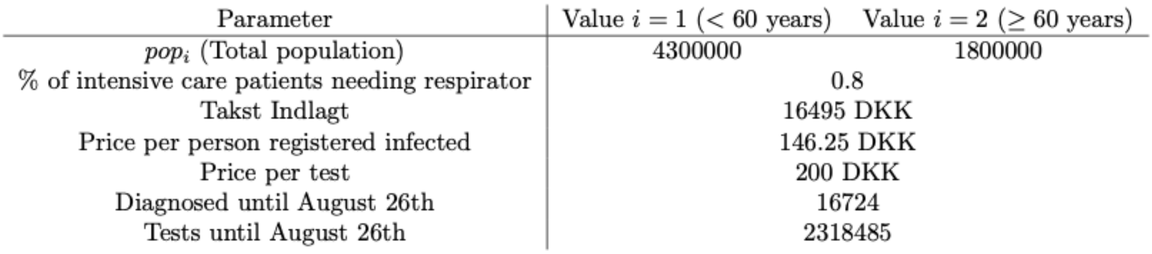
Parameters and initial values used in the SEIR model.

Table A1 Parameters used for bootstrapping



Parameter	Range $i = 1$ (< 60 years)	Range $i = 2$ (≥ 60 years)
$\frac{1}{\gamma_i^{EI}}$	4 – 6 days	
$\frac{1}{\gamma_i^{IR}}$	4 – 6 days	
$\frac{1}{\gamma_i^{IH}}$	6 –10 days	5 – 9 days
$\frac{1}{\gamma_i^{HC}}$	0.5 –2.5 days	0.5 – 1.5 days
$\frac{1}{\gamma_i^{CR}}$	14 – 28 days	
$\frac{1}{\gamma_i^{HR}}$	5 –9 days	5 – 15 days
p_i^{IH}	$0,05 - 0,50\%$	$5,0 - 6,2\%$
p_i^{HR}	$77 - 97\%$	$70 - 90\%$
p_i^{CR}	$70 - 95\%$	$45 - 55\%$
$\frac{1}{\mu_i^C}$	14 – 28 days	
$I0$	40000–70000	5000–14000
RR	0.5–1.5	
β_{ii} March 11 to April 14	0.12–0.22	0.14–0.24
$\beta_{12} = \beta_{21}$ March 11 to April 14	0.02–0.12	
$\frac{1}{2}\Delta\beta_{ii}$ April 15 to May 17	0.0–0.072	0.0–0.022
$\frac{1}{2}\Delta\beta_{12} = \frac{1}{2}\Delta\beta_{21}$ April 15 to May 17	0.0–0.01	
$\frac{1}{2}\Delta\beta_{ii}$ May 18 to May 30	0.0–0.076	0.0–0.057
$\frac{1}{2}\Delta\beta_{12} = \frac{1}{2}\Delta\beta_{21}$ May 18 to May 30	0.0–0.027	
$\frac{1}{2}\Delta\beta_{ii}$ June 1	0.0–0.015	0.0–0.017
$\frac{1}{2}\Delta\beta_{12} = \frac{1}{2}\Delta\beta_{21}$ June 1	0.0–0.009	
$\frac{1}{2}\Delta\beta_{ii}$ June 26 to August 9	-0.15–0.0	-0.086–0.0
$\frac{1}{2}\Delta\beta_{12} = \frac{1}{2}\Delta\beta_{21}$ June 26 to August 9	-0.04–0.0	

Table A2 Further parameters



Parameter	Value $i = 1$ (< 60 years)	Value $i = 2$ (≥ 60 years)
pop_i (Total population)	4300000	1800000
% of intensive care patients needing respirator	0.8	
Takst Indlagt	16495 DKK	
Price per person registered infected	146.25 DKK	
Price per test	200 DKK	
Diagnosed until August 26th	16724	
Tests until August 26th	2318485	

Table A3 Initial values as used in [12]. Here, *Ntot* = *pop*$_1$ + *pop*$_2$, and .* denotes component-wise multiplications. We correct the portion of susceptible individuals according to the vaccination strategy.

$$
\begin{gathered}
H^R(t_0) = (11, 8)^\top / Ntot \\
S(t_0) = (pop - I0)/Ntot - H^R(t_0) - Vac(t_0) \\
H^C(t_0) = (0, 0)^\top \\
C^R(t_0) = (0, 0)^\top \\
C^D(t_0) = (0, 0)^\top \\
R(t_0) = (0, 0)^\top \\
D(t_0) = (0, 0)^\top \\
U(t_0) = 11.3.2020 \\
HCum(t_0) = (29, 30)^\top / Ntot \\
CCum(t_0) = (0, 3)^\top / Ntot \\
E^1(t_0) = (10, 19)^\top / 24. * I0/Ntot \\
E^2(t_0) = (9, 1)^\top / 24. * I0/Ntot \\
E^3(t_0) = (0, 0)^\top / 24. * I0/Ntot \\
I^{R,1}(t_0) = (1, 2)^\top / 24. * I0/Ntot. * ((1, 1)^\top - p^{IH}) \\
I^{H,1}(t_0) = (1, 2)^\top / 24. * I0/Ntot. * p^{IH} \\
I^{R,2}(t_0) = (2, 1)^\top / 24. * I0/Ntot. * ((1, 1)^\top - p^{IH}) \\
I^{H,2}(t_0) = (2, 1)^\top / 24. * I0/Ntot. * p^{IH} \\
I^{R,3}(t_0) = (2, 1)^\top / 24. * I0/Ntot. * ((1, 1)^\top - p^{IH}) \\
I^{H,3}(t_0) = (2, 1)^\top / 24. * I0/Ntot. * p^{IH}
\end{gathered}
$$

Appendix B

Figure B1. Cost-effectiveness plane for hospital cost specification 1 and 2% discounting of Life Years gained.

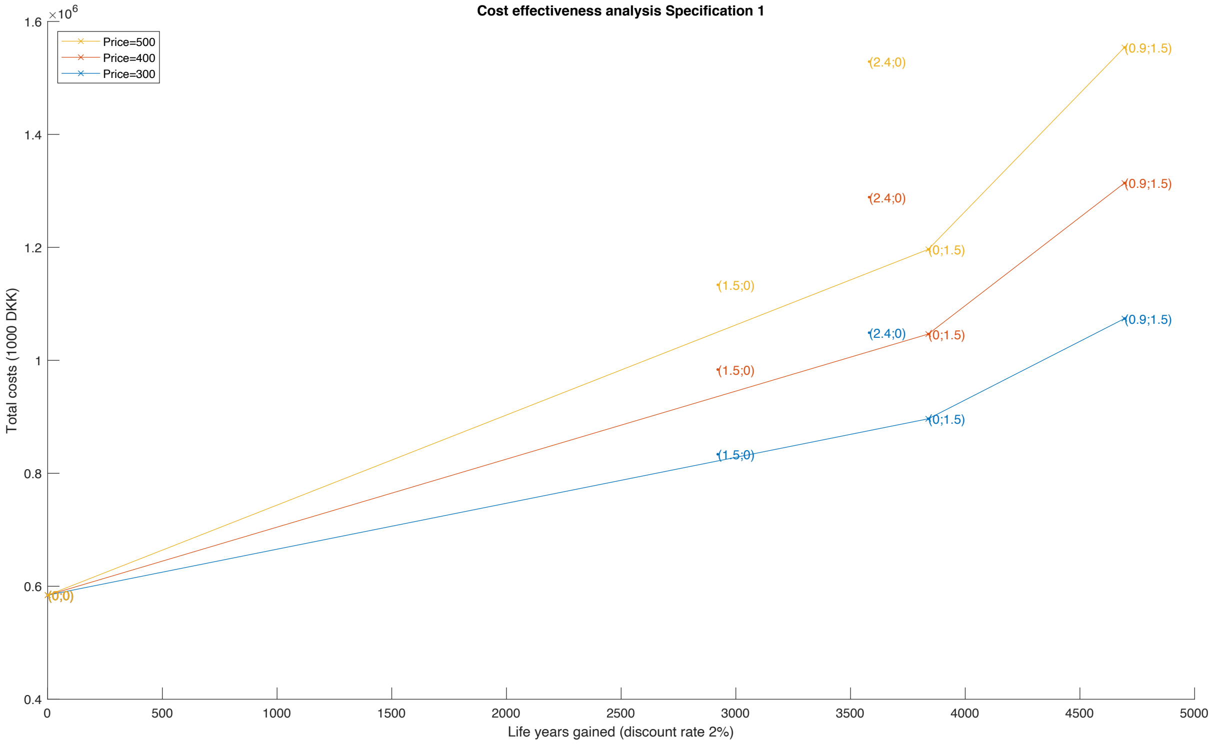
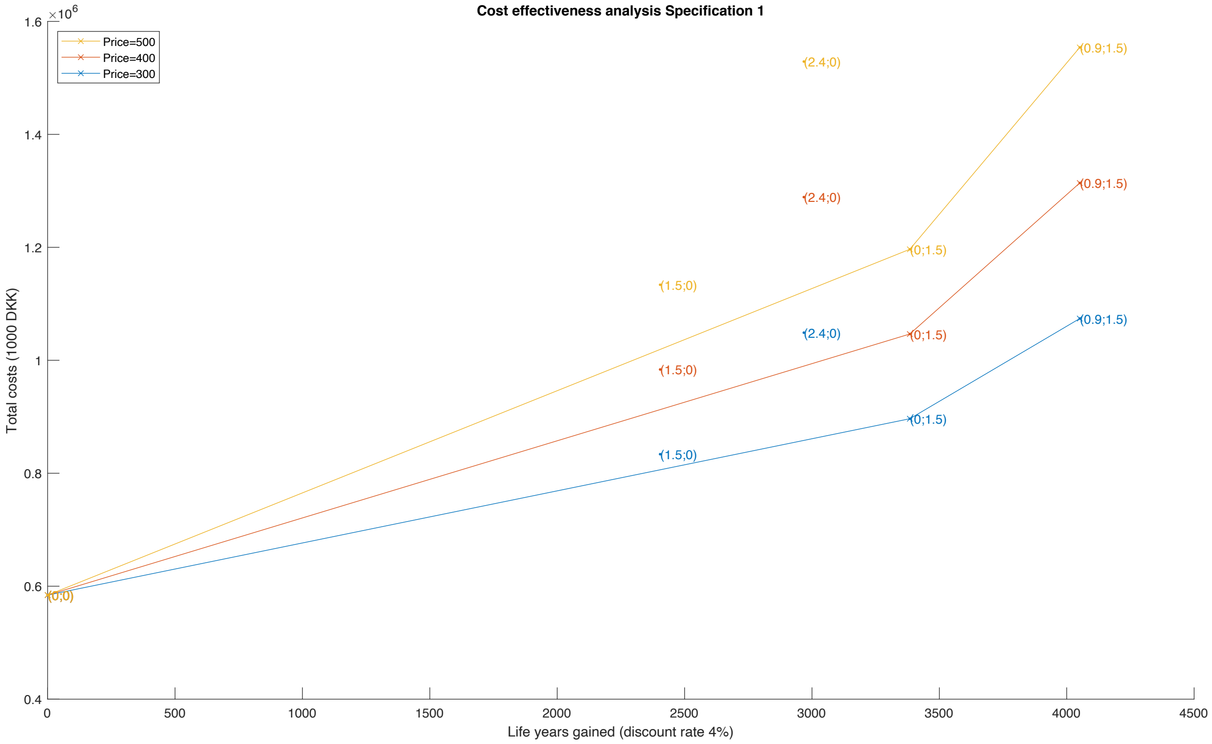


Figure B2. Cost-effectiveness plane for hospital cost specification 1 and 4% discounting of Life Years gained.



Appendix C

Figure C1. Incremental cost-effectiveness ratio for different costs of the vaccination and for gained life years (discounted 2%)

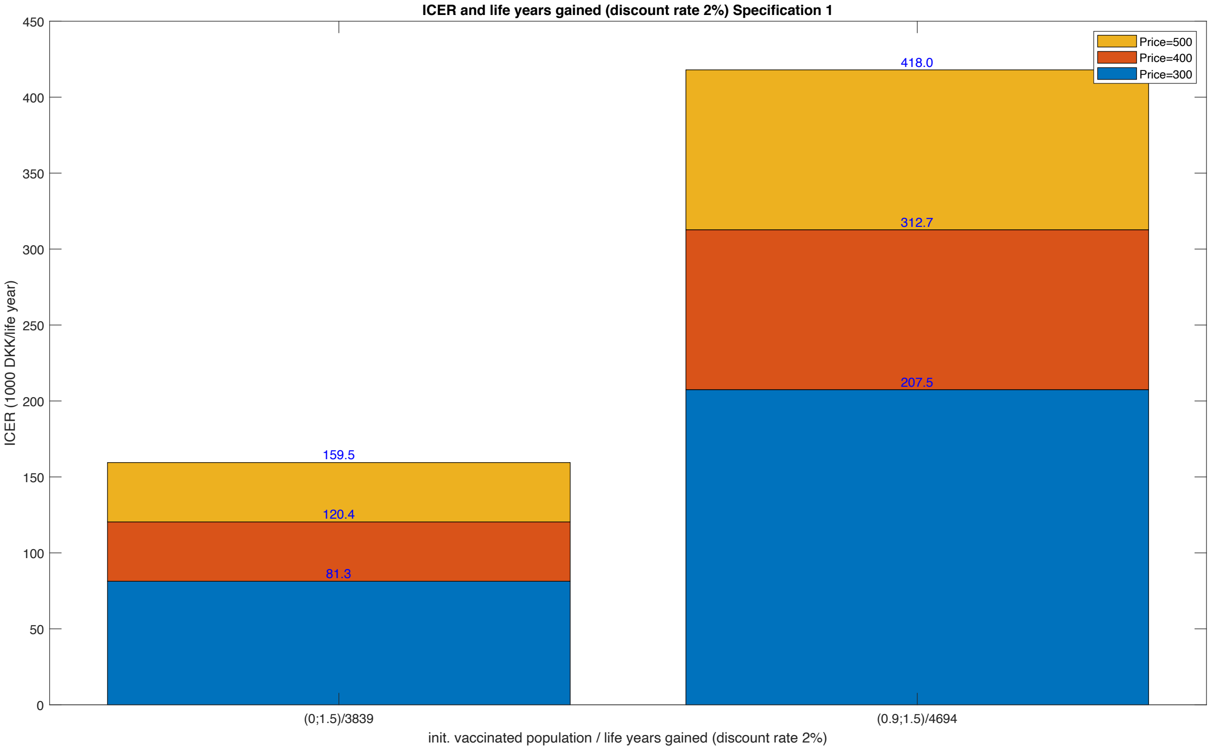


Figure C2. Incremental cost-effectiveness ratio for different costs of the vaccination and for gained life years (discounted 4%)