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YSSP Report
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Optimized testing and lockdown strategies for epidemic control, case COVID-19

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Optimized testing and lockdown strategies for epidemic control, case COVID-19

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Abstract

The ongoing COVID-19 epidemic poses a difficult decision making situation: Too light or late measures to control the epidemic might lead to high casualties and human suffering, too heavy measures might cause economic damage, which in turn can have far-reaching effects on human health and quality of life. Optimization is a widely used technique for dealing with complex decision making situations. Combined with epidemic and economic modeling, it can help decision makers in choosing efficient strategies for epidemic control.

In this work, we propose a modeling approach to support decision making with regards to timing and strength of lockdown and testing measures. The approach combines optimization with a compartmental epidemic model to account for both spread of the disease and the role of testing and interventions, including contact tracing, in mitigating it. We provide a framework for optimizing epidemic control strategies and highlight main implications for the cases similar to COVID-19.

1 Foreword

This report describes the research I completed during the 2020 Young Scientists Summer Program at the International Institute for Applied Systems Analysis. As such, it has limitations in scope and detail of analysis and has not passed peer review. It is my intent to extend this work into a peer reviewed article together with my supervisors.

This work has been performed under the supervision of Dr. Matthias Wildemeersch, to whom I wish to express my warmest thanks for his welcoming attitude and inspiring collaboration. I also wish to thank my PhD supervisor Dr. Eeva Vilkkumaa, who has contributed to this work through critique and discussion.

2 Introduction

The coronavirus disease (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread to nearly every country in the world since it first emerged in China in December 2019. By October 15th 2020, it has caused over 38 million confirmed cases and over one million deaths worldwide. To mitigate further spread of the disease, governments have

adopted different kinds of epidemic control strategies. These strategies can be roughly divided into testing and contact restriction ('lockdown') strategies, and combinations thereof. Testing strategies include contact tracing, testing even slightly symptomatic people, and immunity or antiviral testing. Lockdown strategies include limitations on the operation of schools and non-essential businesses, cancellation of mass events, and issuing stay-at-home orders. Mask wearing regulations can also be counted as lockdown measures.

The extensive testing of the population would make it possible to curb the spread of disease through identifying carriers with little to no symptoms. This would help target isolation and quarantine measures to those people who are known to have the disease or having been exposed to it, which would limit the economic and social impact of these measures compared to large-scale lockdown strategies. Nevertheless, the efficacy of such strategies may be constrained by imperfect testing, i.e., the non-zero probability of obtaining false negative or positive results. Furthermore, testing capacity is often limited by the availability of tests and testing personnel. In the absence sufficient testing capacity during the first wave of the pandemic, countries such as Germany, Finland, and Thailand adopted relatively aggressive lockdown strategies and, consequently, experienced limited numbers of cases and low death rates. Yet, such strategies may cause significant economic damage, which can have far-reaching effects on human health and quality of life. Moreover, as demonstrated by previous studies, the influence of lockdown strategies is highly dependent on the magnitude and timing of such strategies: their impact in terms of controlling the spread of an epidemic is limited if introduced too late or lifted too early.

In view of the above, one of the key questions faced by policy makers during an epidemic is how to choose and implement epidemic control measures in a way that would mitigate the spread of disease while minimizing the economic impact subject to limited testing capacity. The most common approach to studying such questions is to simulate an epidemiological model to assess the impacts of different kinds of control strategies. In epidemiological models, members of the population are assumed to be in a given state or compartment with regard to the epidemic. In SEIR models, for instance, these compartments are susceptible (S), exposed (E), infected (I), and recovered (R). Epidemiological models can be further divided into agent-based and equation-based models. Agent-based models can capture the effects of changes in individual behavior and local interactions on the spread of the epidemic and, thereby, capture high-level patterns emerging from individual behavior (see e.g. [6]).

The main challenge with the use of agent-based models is that they require large amounts of data and are computationally intensive. Consequently, many authors suggest the use of equation-based models, which are more simplified in that they seek to capture average flows between different compartments instead of tracking individuals. Although equation-based models cannot capture the effects of individual behavior, they are rather suitable for studying the impacts of policy changes in cases where reliable data on individual behavior cannot be acquired. Berger et al. (2020)[2], for instance, propose an equation-based SEIR model to evaluate the impacts of simple testing and conditional quarantine policies on the spread of coronavirus, number of deaths caused by Covid-19, and economic output, as measured by the share of overall contribution to the workforce compared to a baseline case where no-one is symptomatic or in quarantine. In doing so, they extend the basic SEIR framework to accommodate incomplete information on whether an asymptomatic member of the population is in fact infected or not. Using this model, they show that testing at a higher rate in conjunction with targeted quarantine policies can (i) dampen the economic impact of the coronavirus and (ii) reduce peak symptomatic infections. Yet, the model assumes that testing is done at a fixed rate with no constraints on testing capacity, and that tests are perfectly accurate (i.e., no false negative or positive results exist).

In the above approaches, epidemic control strategies are not optimized in a mathematical sense,

but rather a few predetermined strategies are compared to one another in terms of their outcomes on relevant objectives. Consequently, such approaches may suggest strategies that are either unaffordable due to a lack of constraint on testing capacity, or suboptimal in that, for instance, testing resources could be reallocated to achieve a better outcome with respect to spread of disease and economic output. Below we highlight some of the approaches used to combine complex systems and optimization.

In case the simulator at hand is stochastic, approaches can fall under Simulation Optimization (SO), where complex simulation models are combined with an optimization methodology to achieve improved, or in some cases optimal performance of the simulated system in a statistical sense. The methods can range from simply comparing simulation runs to recursive and iterative approaches combined with e.g. gradient search methods to evolutionary algorithms. A relatively recent review of state of the art can be found in (Amaran2014).

In (Alistar 2014) the authors were able to optimize a simple HIV epidemic model by exploiting the problem structure and some reasonable assumptions. However, this approach becomes harder to apply as the epidemic model becomes more complex. Oversimplification of the epidemic model may lead to irrelevant or impaired results from application point of view.

Optimal Control Theory can be used to optimize the performance of a continuous or discrete time system through control parameters as in e.g. works by Tragler [8] and Lefèvre [5]. In these models, the spread if the disease and controls are often modeled through differential equations, and the controls are optimized using numerical approaches or analytically.

One way to overcome complexity is to reduce the epidemic model to a metamodel, that can then be optimized using well known optimization approaches, such as stochastic optimization or linear optimization. However, reducing an epidemic into an algebraic model is challenging and still risks losing some of the dynamics of the original model. One example of this kind of approach is in (De Angelis, 2003).

In case the model to be optimized is complex and there is no willingness or reasonable approach to simplify it, one can resort to heuristic optimization. The benefit of using heuristics is that these methods are able to handle complex, even black box objective functions and constraints. In [4], a coupled system dynamics model comprised of differential equations is optimized using pattern search. The result is recommendations for screening and treatment policies for HIV epidemic. Saurabh et al. [7] use the NSGA-II algorithm to minimize deaths and economic impacts through state specific lockdown policies for India.

The contribution of this paper to epidemic control optimization is 3-fold. First, we introduce a multi-objective optimization approach to concurrently optimize timing and strength of control measures in a deterministic epidemic process modeled as a 12-state compartmental model. Second, we introduce imperfect testing and a novel approach to modeling contact tracing (CT) using compartmental models. Finally, we combine these to derive policy insights for COVID-19 type epidemics.

3 Model description

In this section we present our model framework for controlling an epidemic. In particular, Section 3.1 introduces the compartmental model that is used to capture the spread of the epidemic subject to control measures regarding lockdown and testing. In Section 3.2 we formulate a multiobjective optimization problem for optimizing these control measures in view of minimizing the number of deaths, lost working hours, and direct costs. Section 3.3 presents the Non-dominated Sorting Genetic Algorithm II that is used to solve the set of Pareto optimal solutions with respect to the two objectives.

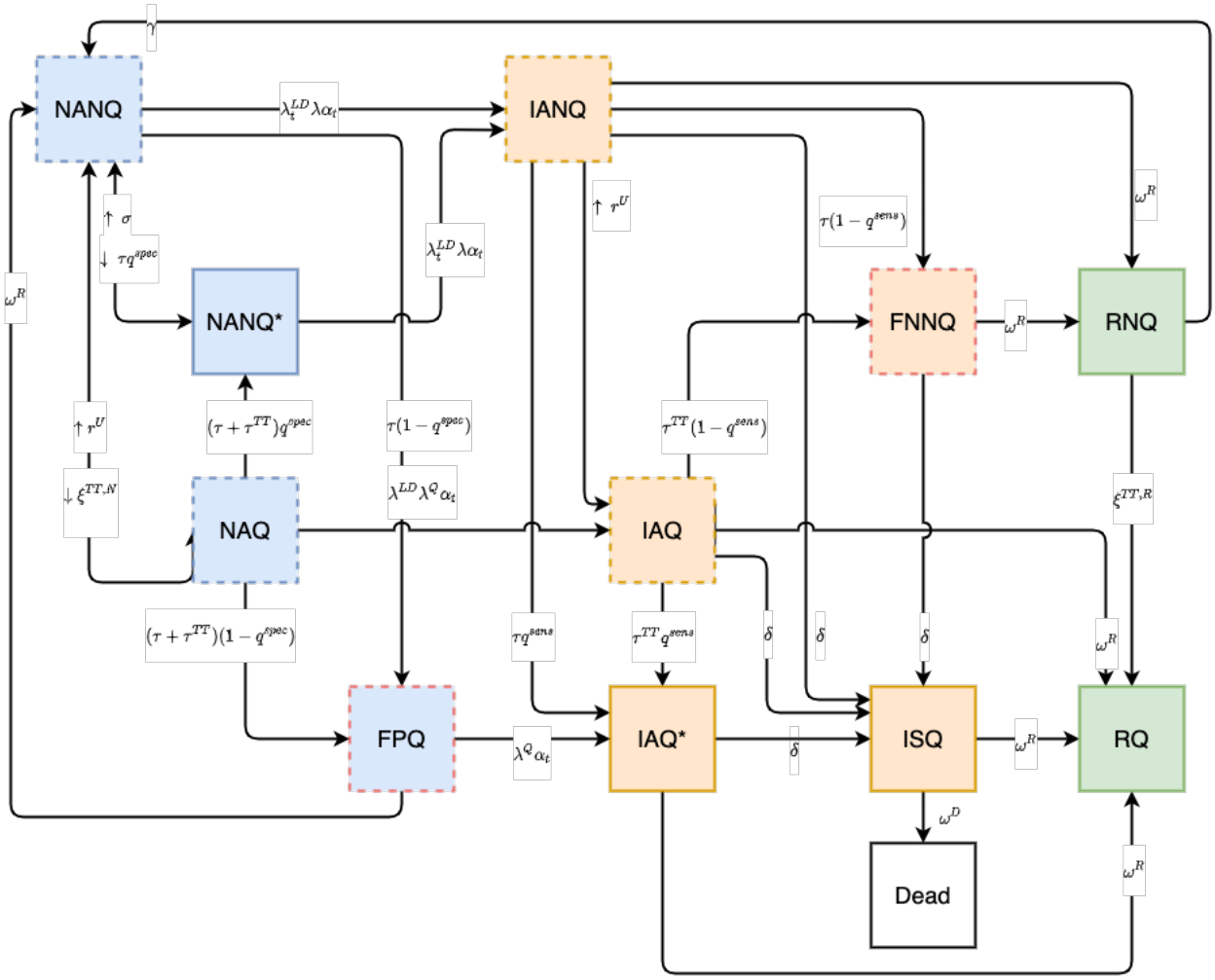

Figure 1: Extended SEIR compartmental epidemic model.

3.1 Epidemic model

Figure 1 illustrates the compartmental model that we use to simulate the progression of the epidemic in different circumstances and with different control measures. This model comprises 12 compartments (depicted in the figure by rectangles, and explained in 2), each of which describes a potential status for a given member of the population in terms of infection, quarantine and information state. Transitions between these compartments are depicted by arrows between the rectangles and formalized mathematically as a transition matrix $\mathbb{T}$ in table 3. The general and transition parameters of the model are listed in tables 1 and 4, respectively.

Table 1: General epidemic simulation parameters (see also 3)

Symbol	value	description
pop	340 000 000	Population. Used mainly for illustrative purposes, based on U.S. population[2]
T_{years}	2	Simulation time in years
$I_{initial}$	300	number of initial infections at $t = 0$

3.1.1 Compartments

Table 2: Compartments in the epidemic model

$NANQ$	Not infected asymptomatic non-quarantined: susceptible to infection but not yet infected. They are not quarantined, so they contribute fully to output. Their status is not known to the healthcare system.
NAQ	Not infected asymptomatic quarantined: susceptible to infection but not yet infected. They are quarantined, so their output is reduced by λ^Q. Their status is not known to the healthcare system.
$NANQ^*$	Not infected asymptomatic non-quarantined, known: susceptible to infection but not yet infected. They are not quarantined, so they contribute fully to output. Their status is known currently.
$IANQ$	Infected asymptomatic non-quarantined: can spread the disease to others. They are not quarantined, so they contribute fully to output and new infections. Their status is not known to the healthcare system.
IAQ	Infected asymptomatic non-quarantined: can spread the disease to others. They are quarantined, so their contribution to output and new infections is reduced. Their status is not known to the healthcare system.
IAQ^*	Infected asymptomatic non-quarantined: can spread the disease to others. They are quarantined, so their contribution to output and new infections is reduced . Their status is known to the healthcare system.
FPQ	False positive: received a false positive result from testing and are thus assumed to be infected by the health care system, even though they are in fact not infected. Due to the positive result, they are quarantined and their contribution to output is reduced.
$FNNQ$	False negative: received a false negative result from testing. Assumed to be non-infectious and are thus not quarantined. Contribute fully to new infections and output.
ISQ	Infected symptomatic quarantined: have an infection and have developed symptoms. Their state is known to the healthcare system and they are quarantined.
RNQ	Recovered non-quarantined: Have been infected and recovered from that infection. They have temporary immunity to new infections.
RQ	Recovered quarantined: Have been infected and recovered from that infection. They have temporary immunity to new infections. Reduced contribution to output.
D	Deceased. Permanently removed from output.

If a person has been tested and is known to be uninfected, we assume that they are not quarantined. Likewise, if a person has been tested and is known to be infected, we assume that they are quarantined. Also, the status of a person who is infected and symptomatic is assumed to be known, whereby this person is quarantined.

Recovery includes a limited immunity period. If symptomatic infected persons do not recover, they die by transitioning to deceased state (D). We only account for deaths due to COVID-19, other causes are excluded. Table 2 includes descriptions of compartments.

3.1.2 Transitions

Transition flows between the 12 compartments are captured by the transition parameters listed in Table 4. The third column of this table contains the base case values. These values can change over time due to, e.g., applied control measures. Unless stated otherwise, we use the base case values in all of our analyses.

The transitions between compartments are shown in 3. The rows represent compartments from which transitions happen to the target compartments, represented by columns. For instance, persons currently in false positive (FP) compartment can move to compartment $NANQ$ at rate ω^R and to $IAQ*$ at rate $\lambda^Q\alpha_t$. The first of these transitions represents a situation where a false positive person has been quarantined, naturally without symptoms, for long enough that they can be assumed recovered and thus will be released. The latter represent the situation where they actually get infected, and become true positives. People can transition to FP from $NANQ$ at rate $\tau(1-q^-)$ (as part of a general testing scheme) and from NAQ at rate $(\tau+\tau^{CT})(1-q^-)$, i.e either after being tested in a general scheme or through contact tracing.

Due to the relative short time horizon, no birth rate nor natural death rate is considered and the sum of all compartments equals N. Let $X(t) = [NANQ(t), NAQ(t), NANQ^*(t), IANQ(t), IAQ(t), IAQ^*(t), FPQ(t), FNNQ(t), ISQ(t), RNQ(t), RQ(t), D(t)]$, then we state dynamics can be written shortly as

$$\begin{aligned} X(t+1) &= \mathrm{SEIR}^+(X(t), X(t-1), X(t-2), \lambda, \tau, \eta) \\ &= \mathbb{T}_t(X(t), X(t-1), X(t-2), \lambda, \tau, \eta)X(t) \end{aligned} \tag{1}$$

3.1.3 Contact tracing

Contact tracing (a.k.a. test and trace) is an epidemic control strategy based on identifying infected persons through symptoms or testing, tracing their recent contacts and quarantining and subsequently testing them. We model this possibility in our epidemic model as described below. As an example, let us consider the case of a non-infected person meeting an infected and soon-to-be-diagnosed person, becoming infected by that person and then traced.

The chance of having met such a person on last time step, conditional on a meeting, is

$$\begin{aligned} \pi_t^{\mathrm{IST}} &= \frac{\delta(\lambda^{\mathrm{Q}}\, M_{t-1}^{\mathrm{IAQ}} + \lambda\, M_{t-1}^{\mathrm{IANQ}})}{M_t^{\mathrm{total}}} \\ \pi_t^{\mathrm{IAT}} &= \frac{\lambda\, M_{t-1}^{\mathrm{IANQ}} \cdot \tau\, q^+ + \lambda^{\mathrm{Q}}\, M_{t-1}^{\mathrm{IA-Q}} \cdot (\tau+\tau^{CT})\, q^+}{M_t^{\mathrm{total}}} \\ \pi_t^{\mathrm{FP}} &= \frac{\lambda\, M_{t-1}^{\mathrm{NANQ}} \cdot \tau\,(1-q^-) + \lambda^{\mathrm{Q}}\, M_{t-1}^{\mathrm{NA-Q}} \cdot (\tau+\tau^{CT})\,(1-q^-)}{M_t^{\mathrm{total}}} \end{aligned} \tag{2}$$

Meeting such a person (out of all meetings) can lead to infections at conditional rate ρ^S, giving an infection rate per random meeting:

$$\alpha_{t-1}^{IS} = \pi_{t-1}^{IST}\rho^S + \pi_{t-1}^{IAT}\rho^A \tag{3}$$

At this point these persons will move to IANQ compartment, at rate:

$$\lambda\alpha_{t-1}^{IS} = \lambda\pi_{t-1}^{IST}\rho^S \tag{4}$$

and the mass calculated below. This mass is the infected mass that can be traced on the next time step. It is a 'compartment within compartment' in IANQ.

$$M_t^{TI} = \lambda(\pi_{t-1}^{IST}\rho^S + \pi_{t-1}^{IAT}\rho^A)M_{t-1}^{NANQ} \tag{5}$$

In our model, this transition happens as part of the total transition from NANQ to IANQ, happening at rate

$$\lambda\alpha_{t-1} = \lambda\pi_t^I[\pi_t^{IS}\rho^S + \pi_t^{IA}\rho^A] \tag{6}$$

Table 3: Epidemic model transition matrix $\mathbb{T}_t$

	$NANQ$	NAQ	$NANQ^*$	$IANQ$	IAQ	IAQ^*	FPQ	$FNNQ$	ISQ	RNQ	RQ	D
$NANQ$		$\xi^{CT,N}$	τq^-	$\lambda^{LD}\lambda\alpha_t$			$\tau(1-q^-)$					
NAQ	r^U		$(\tau+\tau^{CT})q^-$		$\lambda^Q\alpha_t$		$(\tau+\tau^{CT})(1-q^-)$					
$NANQ^*$	σ			$\lambda^{LD}\lambda\alpha_t$								
$IANQ$					$\xi^{CT,I}$	τq^+		$\tau(1-q^+)$	δ	ω^R		
IAQ				r^U		$\tau^{CT}q^+$		$\tau^{CT}(1-q^+)$	δ		ω^R	
IAQ^*									δ		ω^R	
FPQ	ω^R					$\lambda^Q\alpha_t$						
$FNNQ$									δ	ω^R		
ISQ											ω^R	ω^D
RNQ	γ										$\xi^{CT,R}$	
RQ										r^R		

from where they may proceed to IAQ, based on the tracing efficiency η.

This means that only part of the 'new arrivals' , and therefore also only part of the total mass in IANQ are subject to potential tracing efforts. Also, at this point the chance that they have already met an infected person is accounted for (because we know they have, that's how they got infected). Considering the share of these new members in the whole group of infected persons in IANQ leads to transition rate of:

$$\xi^{CT,I} = \eta M_t^{\mathrm{IT}} / M_t^{\mathrm{IANQ}} \tag{7}$$

to IAQ. Fully extended, this becomes:

$$\xi^{CT,I} = \eta \cdot \lambda \rho^S \frac{\lambda^Q(\delta + (\tau + \tau^{CT})\, q^+) M_{t-2}^{IAQ} + \lambda(\delta + \tau\, q^+) M_{t-2}^{IANQ})}{M_{t-1}^{total}} \frac{M_{t-1}^{NANQ}}{M_t^{IANQ}} \tag{8}$$

The same approach can be applied to meeting a newly diagnosed infected person and getting traced but not infected, and for getting traced while being in RNQ, and thus immune:

For the non-infected, the process moves on similarly to the one above. Instead of infection chance, one only needs to consider the complement, and instead of target compartment IANQ, the compartment NANQ. This gives:

$$\xi^{CT,N} = \eta M_t^{\mathrm{NT}} / M_t^{\mathrm{NANQ}}, \tag{9}$$

where

$$M_t^{\mathrm{NT}} = \lambda(\pi_{t-1}^{IST}(1-\rho^S) + \pi_{t-1}^{IAT}(1-\rho^A) + \pi_{t-1}^{FP}) M_{t-1}^{NANQ} \tag{10}$$

The quarantine rates for the recovered are modeled by assuming that they have met the tracing-initiating person while already recovered. This gives:

$$\xi^{CT,R} = \eta M_t^{\mathrm{RT}} / M_t^{\mathrm{RNQ}}, \tag{11}$$

where

$$M_t^{\mathrm{RT}} = \lambda(\pi_{t-1}^{IST} + \pi_{t-1}^{IAT} + \pi_{t-1}^{FP}) M_{t-1}^{RNQ} \tag{12}$$

Another way to formulate this would be to build pass-through compartments for 'traceable' IANQ, NANQ and RNQ that would be kept separate from the 'main' IANQ, NANQ and RNQ compartments. The only transitions to quarantine through test and trace would then be from these 'traceable' compartments with rate η. The remaining population members would transition to the 'main' compartments because their 'traceability' would be lost.

3.2 Optimization model formulation

We consider as objectives the minimization of the number of deaths $\mathcal{D}$ and the economic and healthcare related costs over the considered time horizon $\mathcal{C}$. Let $u = \{\lambda, \tau, \eta\}$, then the optimization problem can be formulated as follows

$$\min_{u \in \mathcal{A}} . \qquad \mathcal{D} = \sum_{t \in T} D(t, \lambda, \tau, \eta) + S_{\mathcal{D}}^T(T, \lambda, \tau, \eta) \tag{13}$$

$$\min_{u \in \mathcal{A}} . \qquad \mathcal{C} = \sum_{t \in T} C_{\mathrm{e}}(t, \lambda, \tau, \eta) + S_{\mathcal{C}}^T(T, \lambda, \tau, \eta) \tag{14}$$

$$\text{subject to} \qquad X(t+1) = \mathrm{SEIR}^+(X(t), X(t-1), X(t-2), \lambda, \tau, \eta) \tag{15}$$

$$N_{tests}(u,t) \leq N_{tests}^{max}(t), \qquad \forall\, t \in T,\ u \in \mathcal{A} \tag{16}$$

$$\tag{17}$$

Table 4: Transition matrix parameter descripitions

Symbol	description	base case	source
Δt	Simulation time step. Current value estimates active hours per day (assumption that no infections while sleeping and otherwise inactive).	14	[2]
ξ_t^U	Quarantine rate for unknown states	0.00	assumed
$\xi_t^{CT,N}$	Contact tracing based quarantine rate for non-infected	$f(t, X)$	estimated (9)
$\xi_t^{CT,I}$	Contact tracing based quarantine rate for infected	$f(t, X)$	estimated (7)
$\xi_t^{CT,R}$	Contact tracing based quarantine rate for recovered	$f(t, X)$	estimated (11)
τ	Testing rate applied to all unknown states	0.0	control
τ^{CT}	Contact tracing based testing rate, applied to those in quarantine states. Cumulative with τ_t	0.0	assumed
λ	Meeting rate for persons not in quarantine or affected by lockdown measures [meetings per time step]	1.0	assumed, [2]
λ^Q	Meeting rate for persons in quarantine	$0.5 \cdot \lambda$	[2]
λ^{LD}	Meeting rate for persons who are affected by lockdown measures	0.0	control
α_t	The probability of infection conditional on meeting a person.	$f(t, X)$	estimated, [2]
σ	Rate of loss of information. Describes the transition rate from known uninfected to unknown uninfected in average number of days.	7.0	assumed
δ	Rate of symptom development in avg number of days.	5.0	[2]
γ	Loss of immunity. Describes the rate at which recovered and immune become susceptible again (i.e. lose their immunity) in average number of days.	180.0	assumed
r^U	Quarantine release rate for unknown states	0.1	assumed
r^R	Quarantine release rate for recovered states	0.98	assumed
q^+	Testing sensitivity, i.e. true positive rate	1.0	chosen (clarity)
q^-	Testing specificity, i.e. true negative rate	1.0	chosen (clarity)
ω^R	Recovery rate for infected in average number of days	14.0	[2]
π^D	Probability of death given symptoms	0.01	[2]
ω^D	Death rate for symptomatics	$\frac{1}{\omega^R \cdot \Delta t} \frac{\pi^D}{1-\pi^D}$	[2]

The economic cost is represented by a loss of the work force and can be written as

$$C_{\mathrm{e}}(t,\lambda,\tau,\eta) = N - \frac{\lambda}{\lambda^{\mathrm{base}}} M^{\mathrm{NQ}}(t,\lambda,\tau,\eta) - \frac{\lambda^{\mathrm{Q}}}{\lambda^{\mathrm{base}}} M^{\mathrm{Q}}(t,\lambda,\tau,\eta) \tag{18}$$

The terminal cost functions $S^{\mathrm{T}}_{\mathcal{X}}(T,\lambda,\tau,\eta)$ cannot be expressed as an approximation of an infinite horizon problem over the interval $[T,\infty)$. This would require the introduction of a discount rate, which is not desirable due to the short time horizon we consider in epidemic control. Assuming a linear recovery after T, we can therefore define terminal cost functions for each objective accounting for the cost that will be incurred after T over the economic recovery time ΔT_{rec}

$$\begin{aligned} S^{\mathrm{T}}_{\mathcal{D}}(T,\lambda,\tau,\eta) &= \frac{\Delta T_{\mathrm{rec}}}{2} D(T,\lambda,\tau,\eta)\,, \\ S^{\mathrm{T}}_{\mathcal{C}}(T,\lambda,\tau,\eta) &= \frac{\Delta T_{\mathrm{rec}}}{2} \Big(N - \frac{\lambda}{\lambda^{\mathrm{base}}} M^{\mathrm{NQ}}(T,\lambda,\tau,\eta) - \frac{\lambda^{\mathrm{Q}}}{\lambda^{\mathrm{base}}} M^{\mathrm{Q}}(T,\lambda,\tau,\eta) \Big)\,. \end{aligned} \tag{19}$$

The assumption of linear recovery for all objectives is clearly a simplification, but allows us to incorporate a consistent logic for all terminal costs.

3.3 Computation of Pareto optimal strategies

To optimize the model above, we used the NSGA-II algorithm distributed in 'pymoo' (Python Multi-Objective Optimization) package for Python programming language [1]. The algorithm starts with a random generated initial set of control vectors (population members) with varied control variables ($\lambda^{LD}(t), \tau(t)$) and estimates the respective death and output objective values by running the simulator. After completing one round with a number of different population members, it selects the best ones (preferring non-dominated solutions) for cross-breeding and mutation thus generating new control vectors (offspring) based on the best performing ones . The process is then repeated with a new population composed of both best performers from the previous population and their offspring. The algorithm then continues until convergence conditions are met or maximum number of generations reached. The last population is considered as proxy for optimal solution. For details, see (Deb et al. 2002)[3]. The main parameters affecting the optimization runs are given in the table 5.

Table 5: Main NSGA-II parameters used in optimization runs.

population size	60	Trial solution population size per generation.
number of offspring	30	number of offspring per generation
mutation	real polynomial with $\eta = 8.0$	Mutation operator for population members:
cross-over	sbx	Crossover operator for population members: real simulated binary crossover with 0.9 probability and $\eta = 10.0$
sampling	real random	Initial population generation sampling
elimination of duplicates	yes	Eliminates duplicate solutions in population
termination criteria	default	pymoo MultiObjectiveDefaultTermination with tolerances for changes at: x_tol=1e-8 (decision variables) cv_tol=1e-6 (constraint violations) f_tol=0.0025 (objectives) nth_gen=5 (checked how often) n_last=30 (using last generations) n_max_gen=2500 (maximum generations) n_max_evals=100000 (maximum evaluations)

4 Case studies and scenarios

To study differences in efficient policies given different decision alternatives, starting conditions and parameter values, we performed case studies with scenarios. The scenarios play the role of sensitivity analysis, and cases describe different control approaches. We study the approaches separately (i.e. only optimizing for lockdown timing and strenght, not testing rate, and vice versa) to understand their individual characteristics. In addition, we generate and study mixed approach strategies, i.e. situations where lockdowns and testing are combined. Combinations of following scenario elements were used case studies:

Epidemic spreads with $\mathbf{R_0 = 4.0}$ (instead of $\mathbf{R_0 = 2.5}$) The basic reproduction number R_0 describes the aggressiveness of the spread of the disease. A larger R_0 implies need for stronger control measures. Especially, it might have implications on usefulness of testing measures, given limited testing resources. It is worth noting that a large infection rate $R_0 = 4.0$ together with the assumption of non-permanent immunity creates a cyclical nature into the epidemic. This cyclical nature complicates analysis of effects of control measures on outcomes.

Test quality High quality tests used to identify infectious persons have high sensitivity and specificity values. However, if the availability or price of these tests is prohibitive, lower quality tests might be an alternative. However, using low sensitivity tests might lead to a high number of unidentified infectious persons being not quarantined.

Testing resources Testing can generally be seen as a win-win solution to epidemic control as long as the required number of tests does not grow too high. Different testing limitations thus imply possibly varying efficient lockdown strategies. Changing testing limitations can also help in estimating the marginal value of testing resources.

Delay in symptoms With COVID-19 like epidemics, symptoms may show only after 2 weeks of becoming infectious. This delay can have significant implications on different quarantine / lockdown strategies and usefulness of testing.

4.1 Case 1: Optimization of timing and strength of lockdown with fixed testing rates

The purpose of this case is to study Pareto optimal lockdown strategies under varying epidemic and fixed (not optimized) testing scenarios. The case corresponds to policies selected by many countries during the COVID-19 epidemic, especially after contact tracing has become unfeasible due to high infection rates.

4.1.1 Lockdown strategy

Figure 2 presents the Pareto fronts for several different scenarios. Each point in the front represents a different strategy. In general, the more lockdown measures are used (in strength and/or in time) the less deaths and output there is and vice versa. The nature of these lockdown strategies is often fluctuating, i.e. they may stay at relatively strong values (lower λ^{LD} but release the lockdown for some time period, or vice versa.

4.1.2 Effects of imperfect testing

The effects of limited general testing, with perfect and imperfect tests, on lockdown performance can also be seen in figure 2. It is worthy to note that whereas use of perfect testing expectedly improves the achievable outcomes, imperfect testing can have a negative impact on outcomes. In the figure, testing with sensitivity and specificity at 75% produces a similar Pareto front than lockdown without any testing. The effect of imperfect specificity seems to be stronger than imperfect sensitivity.

This happens due to the following dynamic: lockdown can be seen as a testing scheme with perfect sensitivity and zero specificity, where $\tau =$ (i.e. the virtual testing rate corresponds to quarantine rate) and all 'tested', whether infected or not, are subject to quarantine measures.

Now, imperfect testing differs from this 'virtual testing' by having lower sensitivity. This means that a share of infected persons goes unnoticed, and can spread the disease with full force. Whether this effect leads to a worse outcome on the spread of the epidemic, depends on the relative strength of lockdown to full quarantine and on sensitivity rate. On the other hand, output is reduced due to false positives, who are quarantined and removed from workforce but not necessarily at as high a rate as in lockdown. The epidemic can therefore be controlled more strongly, due to additional quarantine effect. However, at the same time, achievable output decreases and this cannot be alleviated through lockdown measures.

4.2 Case 2: Mass testing without lockdown

This case represents a control approach that relies solely on testing, with the implicit goal of avoiding economically damaging lockdown measures. Here we use as control variable the 'general testing rate' τ for different pre-selected time intervals and the same objectives as elsewhere. Due to the nature of the case, testing sensitivity and specificity will have strong roles on how effective the strategies can be. As sensitivities, we study the different sensitivity and specificity levels, effects of delay in appearance of symptoms, faster spread of the epidemic modeled through larger R_0 and delay in start of measures.

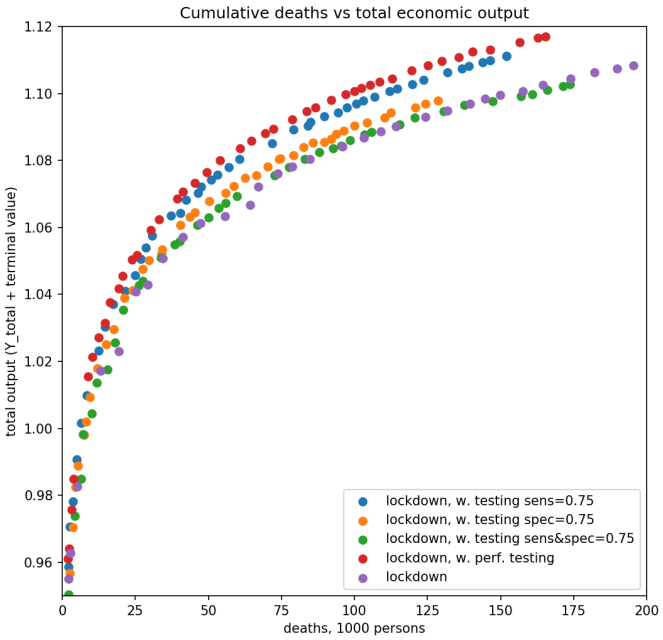

Figure 2: Comparison of achievable outcomes when using lockdown approaches with or without limited testing program with different sensitivity and specificity levels.

4.2.1 Effects of imperfect tests

In figure 3 we see the effects of imperfect testing on deaths and output in this type of testing based control approach. In scenario 'mass testing' perfect testing leads to a situation where there are no trade offs between deaths and output. When sensitivity is imperfect, i.e. < 1.0, we can see that there are still no trade offs but the attainable level of objectives is worse for both than with perfect testing. When specificity decreases, we can see trade offs appearing. This happens because of healthy persons being false diagnosed as positives and quarantined. Even though this quarantining does have some health benefits through healthy population being less exposed to infectious people, the loss in output is strong. This is evinced by the attainable level of deaths being better for imperfect specificity than for perfect tests(!) but the attainable level of output being significantly worse for sensitivity at 0.85.

Policy-wise, the higher quality of testing allows testing measures to be initiated stronger earlier, already when the level of infections within population is lower. In case of low sensitivity, this would lead to high loss of output due to large number of false positives compared to true positives.

4.2.2 Effects of larger R_0

When the epidemic spreads aggresively ($R_0 = 4.0$) the achievable outcomes change, as seen in figure 8. Now, reaching the lowest death levels requires massive testing efforts together with low specificity of tests. In many ways, this compares to a partial quarantine as the low specificity tests push large numbers of people into quarantine as (false) positives (10% of population at maximum when testing limited to 10 million tests per day). This effect can be seen in figure 9 which describes the 'lowest deaths' policies with different sensitivities and specificities. In the beginning of the epidemic, the testing rates are kept low by testing capacity constraint, but increase to use the capacity

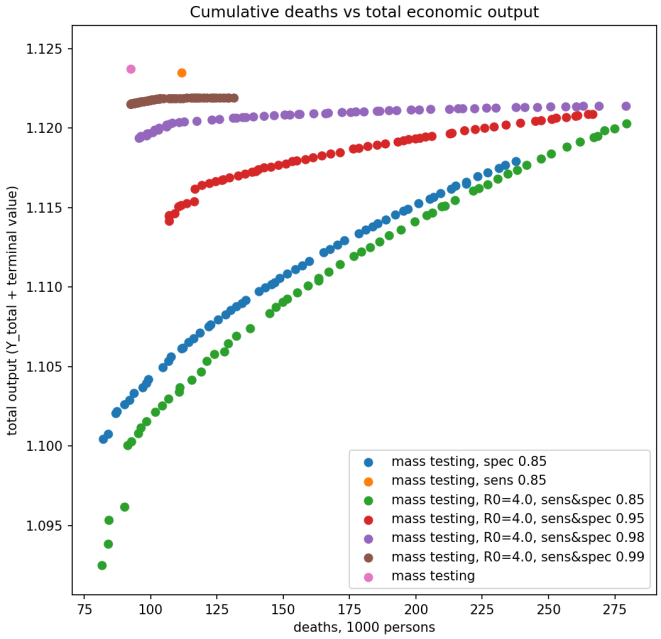

Figure 3: Effects of imperfectly sensitive and specific tests on achievable outcomes in mass testing.

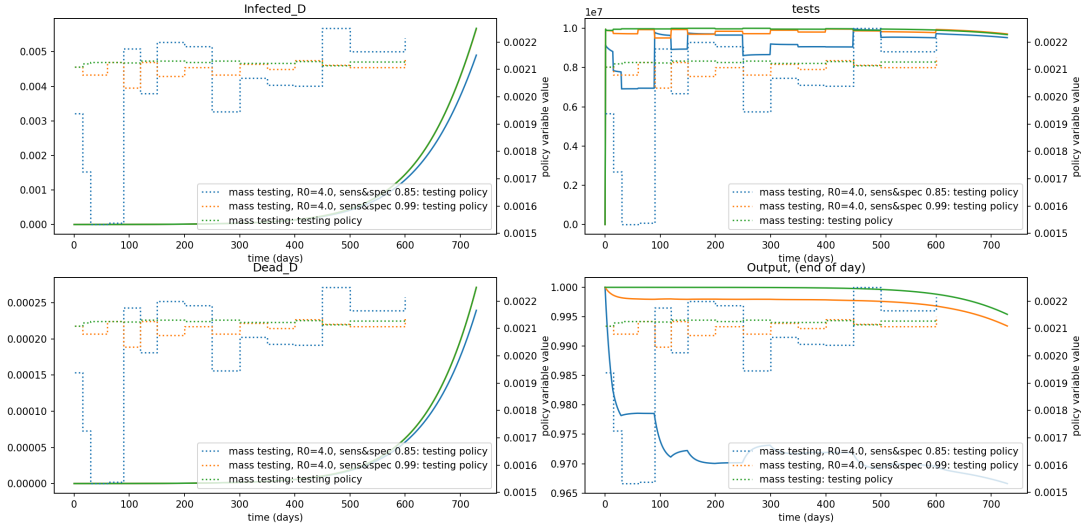

Figure 4: Development of epidemic in 'lowest deaths' policies for mass testing case

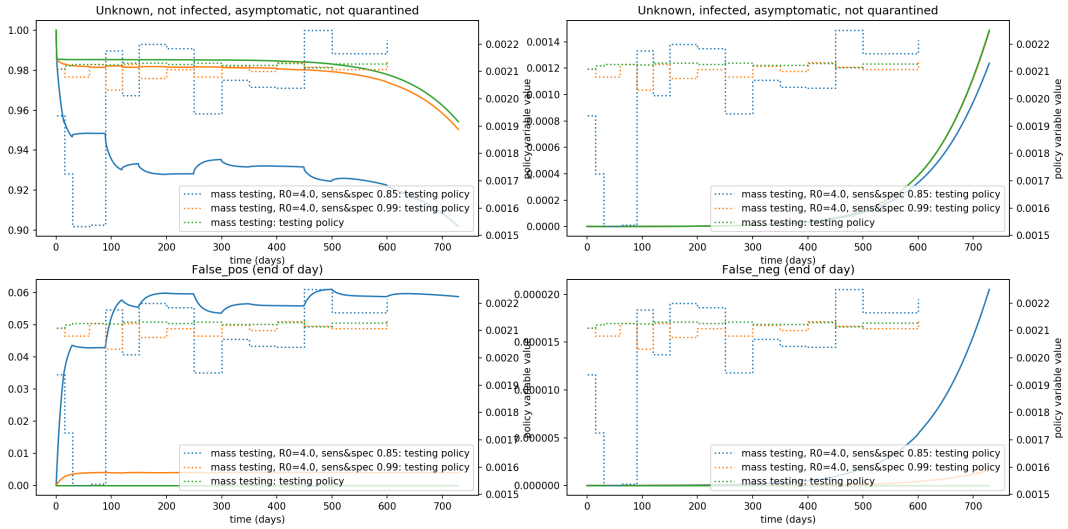

Figure 5: Development of selected compartments for 'lowest deaths' policies in mass testing case.

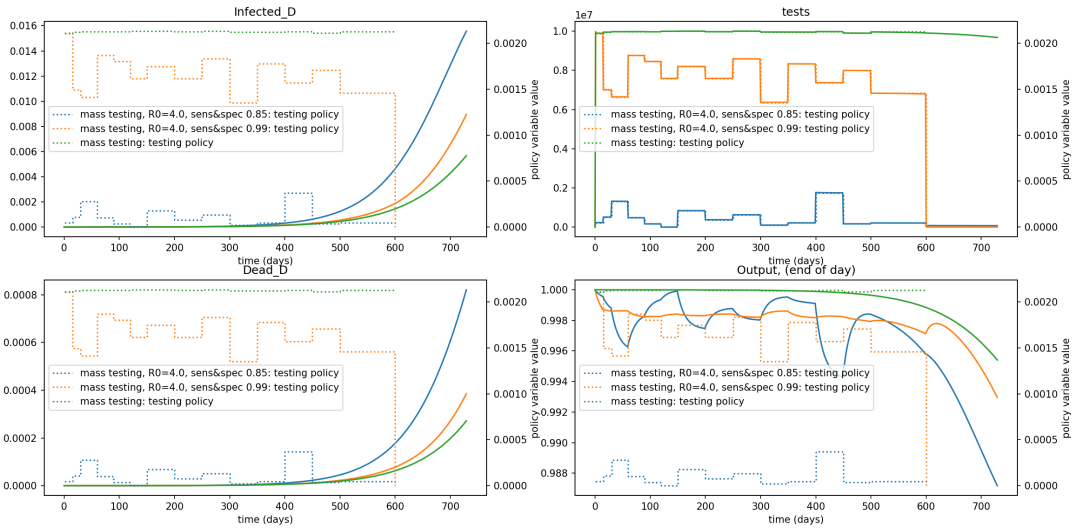

Figure 6: Development of epidemic indicators for 'best output' policies in mass testing case.

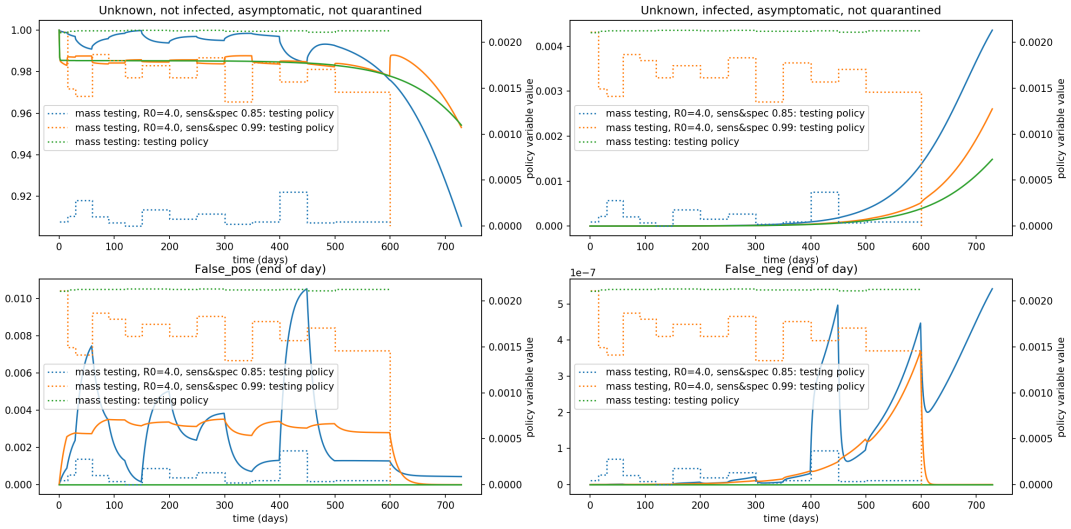

Figure 7: Development of selected compartments for 'best output' policies in mass testing case.

as the population in tested compartments decreases.

4.2.3 Effects of delay in symptoms

As mass testing is best used to detect infected but unsymptomatic persons, it is interesting to study the effect of delay in symptom development. The effects are shown in figure 10. In general, the delay of symptom development improves outcomes. This is caused by asymptomatic infected persons having more time to recover (instead of developing possibly fatal symptoms). This effect also creates a situation where testing more with imperfect tests might lead to low gains in number of deaths but losses in output as people are quarantined.

4.3 Case 3: Contact tracing

We study the performance of contact tracing approach at different efficiency levels η. A summary of results is shown in 11 where we see the clear improvement in epidemic metrics as a η increases. In the $R_0 = 2.5$ scenario, we observe practically complete eradication of the epidemic with 100% tracing efficiency. However, when combined with lockdowns (see figure 12, it seems lockdown effects diminish the effects of CT from achievable outcome perspective.

4.4 Comparison of approaches

What are the differences then between lockdown and testing based epidemic control approaches? In figure 13 we see a comparison between the different approaches, and in figure 14 the same for scenarios with $R_0 = 4.0$. It should be noted that here, the 'mass testing' cases have a limit for maximum testing at 10 000 000 tests per day, implying a daily testing rate of approx 3%, i.e. the whole population could be tested in one month. Even though this can be considered a large testing program, it could in extreme cases be much more extensive. The main limitation on this approach comes from limited testing resources, i.e. allowed number of daily tests, and thus relaxing this constraint would allow significant improvement in testing numbers, as we can see when looking at

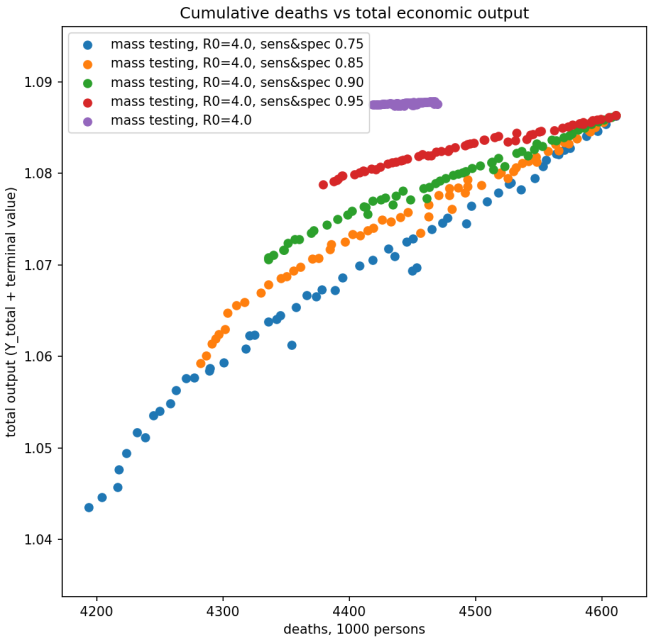

Figure 8: Performance of mass testing approach with different sensitivity and specificity levels with $R_0 = 4.0$

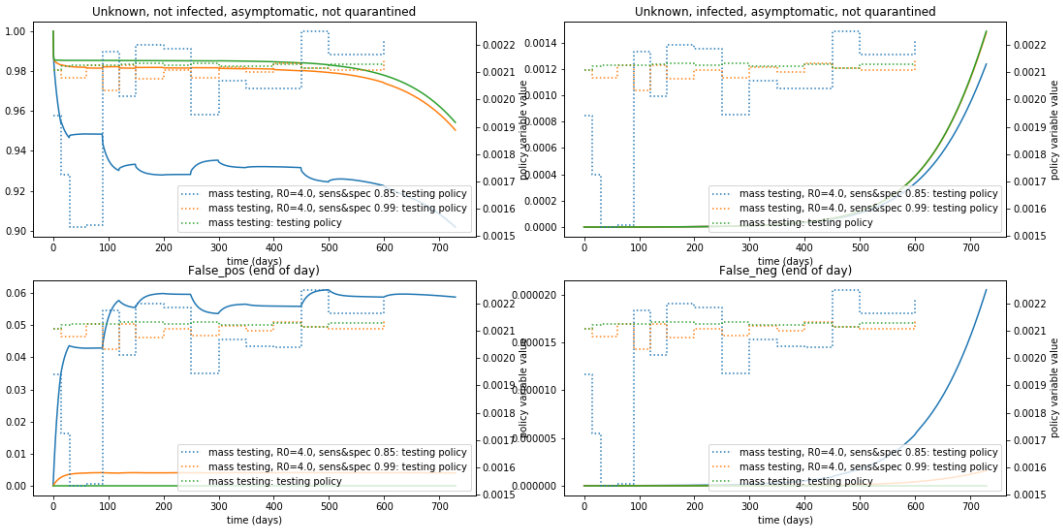

Figure 9: Development of compartments in response to mass testing measures ($R_0 = 4.0$)

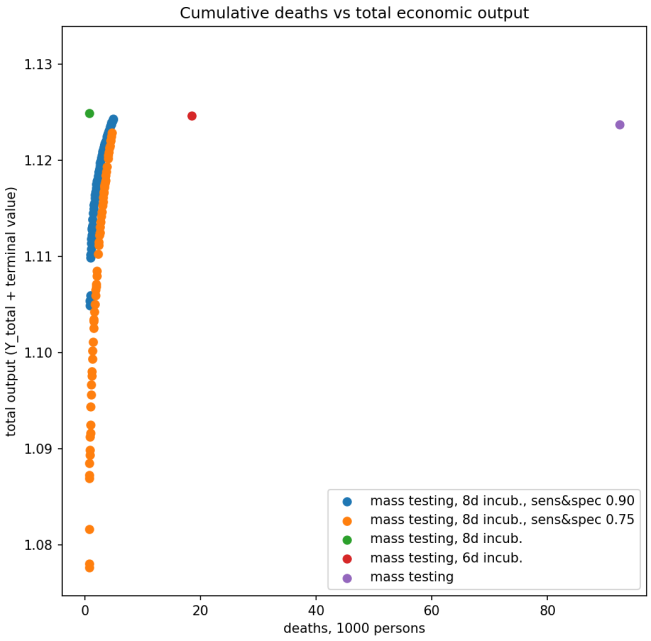

Figure 10: Effects of delay in symptom development to achievable outocomes in mass testing case.

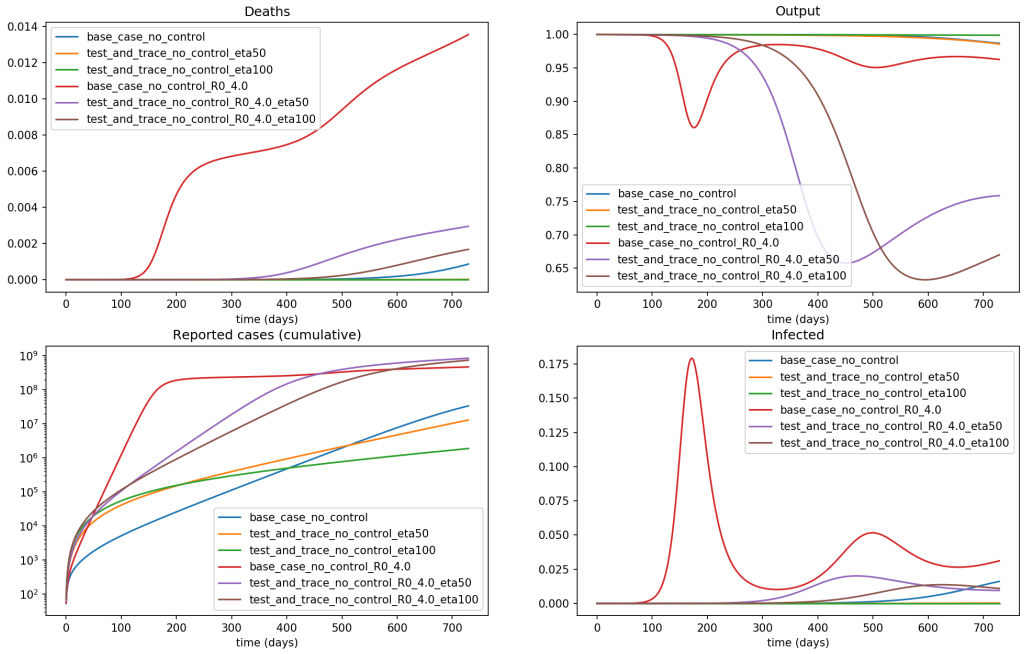

Figure 11: Development of epidemic with contact tracing at various efficiencies.

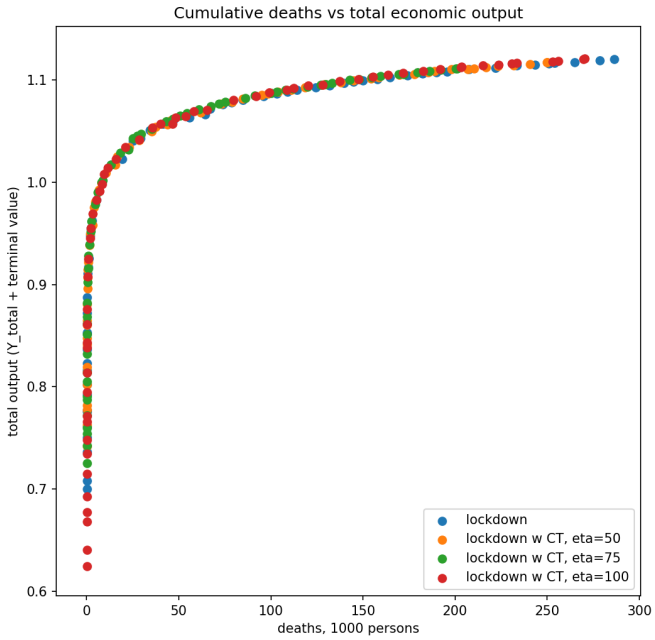

Figure 12: Effect of contact tracing on achievable outcomes in lockdown based epidemic control.

the 'no limit' scenarios. With 10 million daily test constraints in place, the approach cannot reach the same reduction in deaths as lockdown measures that are limited to reducing the meeting rates to 0.5 meetings per person per time step.

5 Policy implications

There are several policy implications implied by the different case results. Due to the nature of modeling, these should be considered as inputs for more detailed modeling or as considerations for decision makers, not as direct recommendations. One possible use case would be to test the performance of policies adapted from these results on more detailed and/or calibrated models.

5.1 Mass testing can be supported by contact restriction

As shown in figure 13, combination strategy practically dominates the other approaches except for mass testing with perfect sensitivity and specificity.

In case of a higher value for R_0, the differences between possible control approaches become relatively smaller. However, approaches utilising testing do fare better than pure lockdown. The effects on achievable outcomes can be seen in figure 14.

5.2 Mass testing is better for economy than lockdowns

Mass testing can improve total output significantly already with limited testing capacity. However, reaching lowest death rates requires large testing capacity. This is seen in figure 13 by comparing cases 'mass testing _no_limit' and 'mass testing', where the maximum testing capacity is set to 10

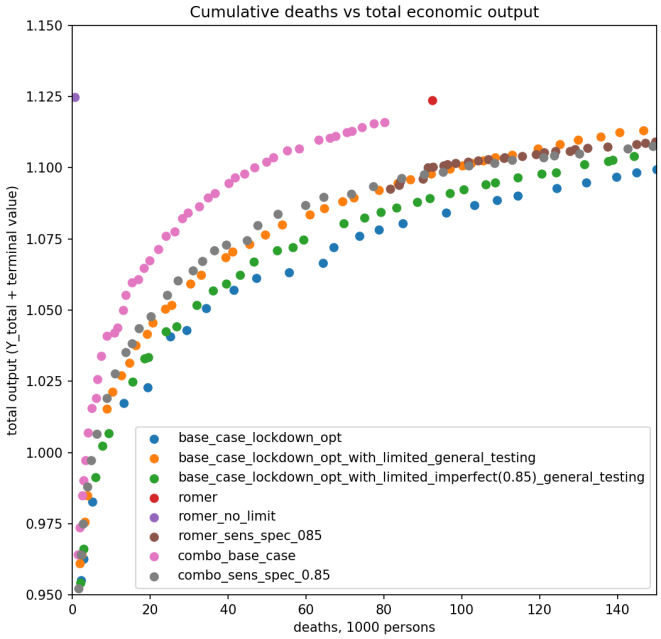

Figure 13: Comparison of performance of different approaches to epidemic control with $R_0 = 2.5$l

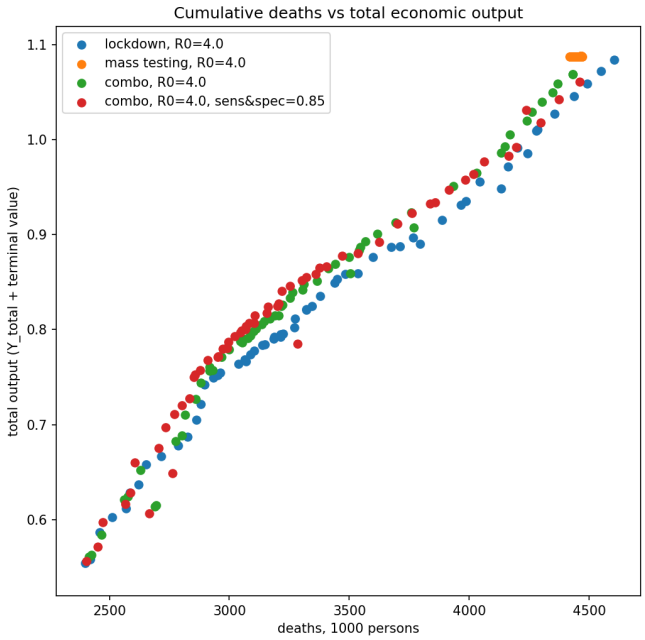

Figure 14: Comparison of performance of different approaches to epidemic control with $R_0 = 4.0$

000 000 daily tests for population of 340 000 000, i.e. at 3%. The testing rates in 'no limit' case translate to testing nearly 25% of population per day.

5.3 Lower specificity tests create trade offs

One interesting observation regarding mass testing schemes is that reducing the specificity of tests actually improves their maximum performance from the death rate point of view, in case of limited testing capacity. This is evinced by lower 'lowest deaths' points in the Pareto fronts for runs with lower specificity. The effect comes from false positives, who are quarantined, thus protecting them from infections. However, at the same time, their output is reduced creating a trade off between deaths and output as a function of testing rate.

The observations imply that decision makers who value health effects have little to gain by mass testing with without large testing resources. Instead, lockdowns or combined approaches might serve their targets better. However, output sensitive decision makers would still choose the mass testing.

5.4 Contact tracing is beneficial by itself, but combining it with lockdowns might dilute benefits

As show in figure 11, applying contact tracing (CT) for the epidemic significantly improves both deaths and output. For using CT in combination with other control measures, we haven't yet been able to show significant benefits (see figure 12. This might be due to the sensitivity of the system to e.g. lockdowns when CT is applied and the optimization algorithms inability to modify the controls in small enough steps. This topic will be researched in more detail in coming publications.

6 Discussion

6.1 Approach

We have presented a methodological framework for heuristic multi-objective optimization of epidemic simulators with constraint on resource use and extended compartmental epidemic simulation by introducing a novel way of modeling contact tracing and imperfect testing.

The strengths of the proposed approach are, that it allows application of multi-objective optimization to a wide range of simulators, optimizing for timing and strength of measures concurrently. Different objectives can be kept separate allowing transparent value decisions on Pareto efficient alternative solutions. The main limiting factor in this approach is the required time and computational resources for a single simulation run, i.e. the complexity of simulation. However, the approach allows heuristic optimization of more complex simulators than many other available approaches. Other limitations are the lack of optimality guarantee and the need for user defined values for multiple optimization parameters (i.e. correct values cannot be derived analytically or from literature).

In application areas such as the one presented in this report where the process that is being modeled, the epidemic, is complex and dynamic, there is often a decision to be made between optimizing a more simplified process with optimality guarantees versus optimizing a more detailed process without optimality guarantees. Our approach contributes to the latter alternative. In this sense, the lack of optimality guarantee should not be considered a critical loss but as allowing the use of more detailed process model, and thus, better correspondence with the real life process.

For many of the parameters that the user needs to set, 'good enough' values can be found through an iterative process. In practice, many of the default values provided within the used pymoo package are acceptable. The computational strain can be helped by using parallel computing resources available through many universities and research organisation, or commercial cloud services.

6.2 Performance and convergence of the NSGA-II algorithm

During all run cases and scenarios, the algorithm reached termination criteria convergence before maximum number of generations (2500) with lower values of R_0. However, in scenarios with $R_0 = 4.0$, convergence was clearly slower and did not reach termination criteria before reaching maximum generations. The observed difference is understandable in the sense that with higher R_0 the effects of controls are stronger, and in this sense, the criteria for termination more strict. This implies, that the presented results for high R_0 might be still improved by longer runs. Also, the 'roughness' of Pareto fronts hints at this possibility.

The different case and scenario runs were run as array jobs on the Triton cluster, part of "Science-IT" project of Aalto University School of Science. Each individual run with max 2500 generations completed depending on convergence, and computation node resources, with maximum runtime of 48 hours 12 minutes (ended at maximum iterations). Different set of optimization parameters could improve convergence, and use of a larger generation limit would allow more time for convergence.

7 Acknowledgements

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