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Impact of asymptomatic COVID-19 carriers on pandemic policy outcomes

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ABSTRACT

This paper provides a mathematical model that makes it clearly visible why the underestimation of r, the fraction of asymptomatic COVID-19 carriers in the general population, may lead to a catastrophic reliance on the standard policy intervention that attempts to isolate all confirmed infectious cases. The SE(A+O)R model with infectives separated into asymptomatic and ordinary carriers, supplemented by a model of the data generation process, is calibrated to standard early pandemic datasets for two countries. It is shown that certain fundamental parameters, critically r, are unidentifiable with this data. A general analytical framework is presented that projects the impact of different types of policy intervention. It is found that the lack of parameter identifiability implies that some, but not all, potential policy interventions can be correctly predicted. In an example representing Italy in March 2020, a hypothetical optimal policy of isolating confirmed cases that aims to reduce the basic reproduction number R_0 of the outbreak from 4.4 to 0.8 assuming $r = 0$, only achieves 3.8 if it turns out that $r = 40\%$.

1. Introduction

Three characteristics of COVID-19 made it a particularly difficult emerging infectious disease to mitigate: high dispersion (meaning a small number of individuals are extraordinarily high viral shedders), infectious presymptomatic carriers and infectious asymptomatic carriers. While many asymptomatic infectious diseases are known, see Potasman (2017) for a review, the standard public health policy for an emergent disease, namely isolation and contact tracing for symptomatic patients, is also known to not perform well when there is a high fraction of asymptomatic carriers (ACs). However, in early 2020, influential experts specifically downplayed the importance of ACs as transmitters of respiratory-borne viruses. Consequently, as recounted in Flaxman et al., (2020), isolation policies were forcefully applied during the early stage of COVID-19 in a number of countries but were quickly found to be inadequate, and were followed by onerous but more effective policies such as lockdowns that targeted the general population. Oran and Topal, in Oran and Topol (2021), argue that this underestimation of ACs combined with an over-reliance on isolation policies was a “catastrophic blunder”. These observations motivate our goal in this paper, which is to apply standard tools from mathematical epidemiology to make the effect of asymptomatic

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Table 1
Estimation of asymptomatic rate r of COVID-19 from various researchers between February 2020 to December 2020.

Date	Sources	Estimation of r
February 2020	China CDC Weekly Report (2020)	1.2%
February 2020	Mizumoto et al., (2020)	17.9% (15.5–20.2%)
May 2020	Treibel et al., (2020)	1.1% - 7.1%
May 2020	Nishiura et al., (2020)	30.8% (7.7%–53.8%)
May 2020	Arons et al., (2020)	0%–6%
June 2020	Gudbjartsson et al., (2020)	5.7%–58.3%
August 2020	Jia et al., (2020)	58.9% - 92.5%
September 2020	Oran & Eric (2020)	40%–45%
December 2020	Byambasuren et al., (2020)	17% (14%–20%)

carriers on health policy outcomes clearly visible. Then we point out ways these quantitative methods can help to avoid catastrophic blunders of this type in any future emerging diseases.

These health policy difficulties early in 2020 led to awareness and interest in asymptomatic COVID-19 infections, and in particular the difficulty in establishing their prevalence. Table 1 shows the wide range of values of r, the fraction of SARS-CoV-2 carriers that are asymptomatic, published in studies early in the pandemic. A metastudy Oran & Eric (2020) gives a comprehensive summary of these results, and based heavily on three studies with large, representative samples of a population, concludes that r likely exceeds 30%. The same paper also provides the Definition of "asymptomatic" we adopt here: "The asymptomatic individual is infected with SARS-CoV-2 but will never develop symptoms of COVID-19. In contrast, the presymptomatic individual is similarly infected but eventually will develop symptoms." References such as Bai et al., (2020), Chan et al., (2020), Hu et al., (2020), Wang et al., (2020). Li et al., (2020) point to the dangers arising from silent carriers who are likely to socialize much more than symptomatic patients.

To clarify the effectiveness of possible large scale non-pharmaceutical interventions (NPIs) early in the epidemic, we introduce a simplified scenario of a country in which no effective policy measures are undertaken until a certain date early in the epidemic, called the policy time T_P. We then compare outcomes at a later date that result from different combinations of NPIs implemented on that date. We imagine that the policy makers are unaware or uncertain about asymptomatic carriers, and investigate how this uncertainty might influence the success of the policy. We consider kinds of NPIs that have been proposed in the literature and implemented in practice. For example, Fraser et al., (2004) recommends the isolation of symptomatic patients and their contacts, and Wu et al., (2006) provides recommendations for household-based public health interventions. Sarah et al., (2020) discusses the effect of asymptomatic patients on the demand for health care and Bousema et al., (2014) discusses public health tools that can be used to deal with the presence of asymptomatic carriers. Ferguson et al., (2006) apply large scale agent-based simulations to analyze the effect of public health policies on the spread of a virus in its early stages. Our policy setting is modeled using tools of mathematical epidemiology. The SE(A+O)R model we use is a simple variant of the standard susceptible-infective-removed (SIR) compartmental ordinary differential equation (ODE) model introduced in Ogilvy Kermack and McKendrick (1927) that splits compartment I into A (asymptomatic carriers) and O (ordinary carriers), and includes a compartment E (exposed) to represent the latent phase of the disease before the onset of infectiousness. Details about compartmental epidemic models can be found in Hethcote (2000), Contreras et al., (2020), Yang et al., (2020). To distinguish the actual state of the disease from what we observe about it, we additionally assume our observations of the disease include a system of testing that generates a daily time series (C_t, D_t) of the number of active confirmed cases and confirmed deaths. This data, combined with parameter estimates from known studies of COVID and human behaviour, will lead to estimates of the *actual state* $(S(t), E(t), O(t), A(t), R(t))$ of the disease as continuous functions of time t.

This paper makes two main contributions. First, it presents a standard epidemiology model that leads to a simple linear regression for the relation between confirmed case count data and the actual dynamical state of the disease, highlighting the sensitivity of this relation to the uncertain parameter r. Second, it presents a general framework for computing the impact of different policies on the actual state of the disease, and in particular gives a closed formula for the basic reproduction number R_0 that results from any combination of policies. These formulas show that the standard isolation policy that targets only confirmed cases will be ineffective if r is higher than expected, while population wide interventions such as social distancing or mask wearing are insensitive to the value of r and may be much more effective.

The structure of the paper is as follows. Section 2 analyzes the properties of the SE(A+O)R model for the actual dynamical state of the disease, in which infectives (I) are separated into asymptomatic carriers (AC) and ordinary carriers (OC). The SE(A+O)R state process is supplemented with a model for the observation process in Section 3. The resultant hybrid model is then calibrated to publicly available data for the early stages of the disease in two countries, Canada and Italy, prior to any nation-wide policy implementation. In Section 4, we prove and illustrate our main results on the efficacy of four types of public health intervention: isolation of infective patients, social distancing, personal protective equipment, and hygiene. Finally, in Section 5, we argue that our main conclusions, proved in a simple model, are likely to hold under much weaker assumptions. In particular, we identify which data gaps need to be filled in order for formulas of the type derived here to be confidently used for predicting actual policy outcomes.

2. The SE(A+O)R model

This paper will model the actual dynamics of the disease with a variation of the standard SIR ordinary differential equation (ODE) model that splits the infectious compartment I into two disjoint sets, asymptomatic viral carriers (AC) and ordinary carriers (OC), and includes a compartment E (exposed). To account for the limited amount of testing that was possible early in the pandemic, it is also assumed that only a fraction of "actual" cases will be counted as "confirmed".

2.1. Asymptomatic and ordinary carriers

At the time of writing, there continues to be uncertainty about the prevalence of AC in the general population, in part because of different definitions of what is meant by an AC. We adopt the Definition of Oran & Eric (2020), which does not depend on whether or not the case has been tested or otherwise confirmed:

Definition 1.

1. *An Asymptomatic Carrier (AC) is someone who*
   (a) *has been exposed to COVID and is currently infectious;*
   (b) *will show no noticeable COVID symptoms for the entire infective period.*
2. *An Ordinary Carrier (OC) is someone who*
   (a) *has been exposed to COVID and is currently infectious;*
   (b) *will show some noticeable COVID symptoms at some point during the entire infective period.*

Remarks 1. *Note that presymptomatic carriers and carriers with mild symptoms are included in OC, as long as they eventually show recognizable symptoms.*

With Definition 1, AC individuals are unlikely to be identified and confirmed, leading to great uncertainty in their prevalence. Moreover, various studies define the term "asymptomatic" differently. These intrinsic difficulties make it problematic to determine the key parameter, the *asymptomatic fraction r*, which we define to be the fraction of exposed individuals who remain asymptomatic. We assume that r is an intrinsic characteristic of the infection mechanism, but its value may differ greatly from studies that adopt a different definition. Table 1 displays estimates of r made in a number of studies and metastudies prior to mid 2020. We see that the value sharpened somewhat over 2020, but still remained very uncertain. The appearance of new COVID-19 variants in late 2020 has further clouded the picture.

The metastudy Oran & Eric (2020) is the most conclusive reference. Their important message summarizes the situation: "On the basis of the three cohorts with representative samples—Iceland and Indiana, with data gathered through random selection of participants, and Vo', with data for nearly all residents—the asymptomatic infection rate may be as high as 40%–45%. A conservative estimate would be 30% or higher to account for the presymptomatic admixture that has thus far not been adequately quantified."[1]

2.2. System assumptions

In this section, we specify the basic SE(A+O)R model for a fully homogeneous well-mixed population, applicable in a jurisdiction before any significant COVID mitigation response has been initiated.

Assumptions 1.

1. *The total population $N = S(t) + E(t) + A(t) + O(t) + R(t)$ is constant. We neglect natural births and deaths by setting the natural birth and death rates equal to zero, and neglect immigration or emigration.*
2. *The removed compartment includes the recovered population who acquire permanent immunity and all COVID deaths. No vaccine is yet available for the virus, which means all people are susceptible prior to their first exposure.*
3. *The population is homogeneous and well-mixed, and thus the mass-action principle is assumed for the infection transmission. Both the latent period (exposed and not yet infectious) and infectious period are exponential random times.*

Remarks 2. *It is common modelling practice to extend the ODE approach to allow for $M > 1$ communities, with the homogeneous and well-mixed assumption within each community. It is also common practice to model the latent and infectious periods as random times with a more realistic gamma distribution. Finally, one can extend such a modelling framework to capture more complex transmission dynamics of COVID 19 by separating the compartment (O) into subcompartments with differing levels of symptoms and infectivity.*

[1] The same authors later published an extended metastudy Oran and Topol (2021) that further validates their conclusion

Table 2
Notation.

S	Susceptible population
E	Those exposed to COVID-19 but not yet infectious
O	Ordinary carriers
A	Asymptomatic carriers
R	Removed population
α^O	Transmission rate of Compartment (S) from Compartment (O)
α^A	Transmission rate of Compartment (S) from Compartment (A)
β	Inverse duration time in Compartment (E)
γ^O	Inverse duration time in Compartment (O)
γ^A	Inverse duration time in Compartment (A)
r	Fraction of (E) that become (A)

Based on these assumptions and using the notation identified in Table 2, the SE(A+O)R model is defined by the following system of ODEs:

$$\begin{aligned}
\frac{dS}{dt} &= -\left(\alpha^O O + \alpha^A A\right) S \,, \\
\frac{dE}{dt} &= \left(\alpha^O O + \alpha^A A\right) S - \beta E \,, \\
\frac{dA}{dt} &= r\beta E - \gamma^A A \,, \\
\frac{dO}{dt} &= (1-r)\beta E - \gamma^O O \,, \\
\frac{dR}{dt} &= \gamma^O O + \gamma^A A.
\end{aligned} \tag{1}$$

2.3. Model parameters

Knowing the meaning of the model parameters is important to understanding the type of data that will be needed to determine them, and how potential policy interventions act.

1. *The asymptomatic fraction r*, the focal point of this paper, remained undetermined and largely ignored early in the pandemic.
2. *Transmission parameters* $\alpha = \kappa\, z\, \tau$ are a product of three parameters that arise in agent-based models (ABMs) and network models, as described in Hurd (2021). In general, α^A, α^O are the average daily rate of new exposures that occur, per susceptible, per asymptomatic or ordinary infectious carrier.
   - $\kappa = \kappa^O = \kappa^A$ is defined as the average number of significant social relations per individual. It is based on studies of normal social conditions, and its value is assumed to not change under any policy intervention.
   - z is the daily rate of "close contacts" per significant social relation. It naturally changes over time, especially when an individual becomes symptomatic or otherwise engages in social distancing.
   - Infectivity τ is the probability that a close contact with an infective person actually leads to exposure (hence the disease). This can be reduced by policies that either boost immunity or reduce viral transfer.
   - Calibration of the SE(A+O)R model to confirmed daily new case data will determine the pre-policy values of α^O, α^A only if both r and the ratio $\rho := \alpha^A/\alpha^O$ are also specified. For discussion purposes we take as a benchmark an ad hoc value $\rho = 4$ resulting from $\tau^A = \tau^O$, $z^A = 4z^O$, meaning that prior to policy interventions, asymptomatic carriers are naturally much more sociable and similarly infectious compared to ordinary carriers.
3. COVID-19 studies made during the early stages of the pandemic, notably Li et al., (2020), Lauer et al., (2020), Tuite et al., (2020), suggest that the average latent period is about 5 days and the average infectious period is about 6 days. In view of the difficulty to observe asymptomatic cases, it is reasonable to assume that the average infectious period for both asymptomatic and ordinary cases are equal. Under the exponential time assumption, these values justify the estimators for β, γ^O, γ^A we will use throughout this paper:

$$\hat{\beta} = \frac{1}{\text{Latent Period}} = 0.2 \,, \quad \hat{\gamma}^O = \hat{\gamma}^A = \frac{1}{\text{Infectious Period}} = 0.167 \tag{2}$$

2.4. Linearized analysis

The early stages of the COVID-19 pandemic can be well understood by the linearization of (1) about the disease-free equilibrium (*N*, 0, 0, 0, 0). Under our standing assumption $\gamma^A = \gamma^O = \gamma$, this reduces to a 3-d linear system with state vector $X(t) = (E(t),A(t),O(t))'$:

$$\begin{pmatrix} dE/dt \\ dA/dt \\ dO/dt \end{pmatrix} = \begin{pmatrix} -\beta & \alpha^A N & \alpha^O N \\ \beta r & \gamma & 0 \\ \beta(1-r) & 0 & -\gamma \end{pmatrix} \begin{pmatrix} E \\ A \\ O \end{pmatrix} := B \begin{pmatrix} E \\ A \\ O \end{pmatrix}. \tag{3}$$

Any solution vector $X(t) = (E(t),A(t),O(t))'$ of (3) generates an approximate solution of (1) by setting

$$R(t) = R(0) + \gamma \int_0^t (A(s) + O(s))\, ds\ , \quad S(t) = N - E(t) - A(t) - O(t) - R(t). \tag{4}$$

that will be sufficiently accurate as long as $S(t)/N$ is sufficiently close to 1.

The spectral properties of the matrix *B* can be summarized by the three eigenvalue-eigenvector pairs:

$$\lambda_+\ ,\ V_+ = \begin{pmatrix} 1 \\ rv_+ \\ (1-r)v_+ \end{pmatrix}; \quad \lambda_-\ ,\ V_- = \begin{pmatrix} 1 \\ rv_- \\ (1-r)v_- \end{pmatrix}; \quad -\gamma\ ,\ V_\gamma = \begin{pmatrix} 0 \\ 1 \\ -\alpha^A/\alpha^O \end{pmatrix} \tag{5}$$

where

$$\lambda_\pm = -\frac{\beta+\gamma}{2} \pm \sqrt{\frac{(\beta-\gamma)^2}{4} + \alpha^{\text{eff}}\beta N}, \quad v_\pm = \frac{\beta + \lambda_\pm}{\alpha^{\text{eff}} N}. \tag{6}$$

Furthermore, the *basic reproduction number* ("R-naught") is

$$R_0 = \frac{\alpha^{\text{eff}} N}{\gamma}. \tag{7}$$

It is extremely important that $\lambda_\pm$ and R_0 depend only on $\alpha^{\text{eff}} := (1-r)\alpha^O + r\alpha^A$.

Our primary interest will focus on cases of a pandemic with $R_0 > 1$ which is equivalent to $\lambda_+ > 0 > \lambda_-$. In such situations, the general solution $X(t) = (E(t),A(t),O(t))'$, $t \geq 0$ of (3) with any positive initial small COVID infection has the form

$$X(t) = a_1 e^{\lambda_+ t} V_+ + a_2 e^{\lambda_- t} V_- + a_3 e^{-\gamma t} V_\gamma \tag{8}$$

for coefficients a_1, a_2, a_3, and will exhibit an exponentially fast convergence to a multiple of the dominant eigen solution

$$X_+(t) = (1, rv_+, (1-r)v_+)' e^{\lambda_+ t}. \tag{9}$$

This dominant solution $X_+(t)$ describes the early exponentially growing phase of the pandemic, with $A(t)$, $O(t)$ in a constant ratio r: $(1-r)$. Such constant ratio solutions exist for the full non-linear system (1) as the following easily-proved result implies:

Proposition 2. *Suppose $\gamma^A = \gamma^O := \gamma$ and the initial conditions for (1) satisfy $A(0) : O(0) = r : (1-r)$. Then a constant ratio solution of (1) is obtained by setting $A(t) = rI(t)$, $O(t) = (1-r)I(t)$ for all t from any solution of the following reduced model*

$$\frac{dS}{dt} = -\alpha^{\text{eff}} SI\ , \quad \frac{dE}{dt} = \alpha^{\text{eff}} SI - \beta E\ , \quad \frac{dI}{dt} = \beta E - \gamma I\ , \quad \frac{dR}{dt} = \gamma I \tag{10}$$

where $\alpha^{\text{eff}} := (1-r)\alpha^O + r\alpha^A$.

Linearized analysis of (1) in a neighbourhood of a constant ratio solution identified in Prop 2 shows it will be a stable attractor of more general solutions. This suggests they represent the typical behaviour of the non-linear system, and thus in the following we focus on constant ratio solutions.

2.5. Time periods

Let $t = 0$ denote time 00:00 on January 1, 2020. We assume that the dominant solution (9) of the linearized ODE model is an acceptable approximation for a given country after T_1, called the *pandemic time*, defined as the start of the first day the confirmed cumulative cases exceeded 50 cases. We first study the *pre-policy period* $[T_1, T_2]$ ending at T_2, which is the *policy time* when the first nation-wide policy intervention occurs. Because policy changes taking place at T_2 take several days to have an observable effect on case numbers, we fit the parameters of our model to the *calibration period* $[T_1, T_2 + 5]$. This sets the scene for Section 4, where we will study the effect of possible public health policy interventions implemented at the policy time T_2 for the six-weeks long *post-policy period* $[T_2, T_3]$ with the *end time* $T_3 = T_2 + 42$.

In different countries around the world, the pandemic time T_1 and policy time T_2 typically occurred in February and March 2020. In this paper, we focus for illustrative purposes on Italy and Canada that saw large scale interventions on March 10 and March 15 respectively. These dates are summarized in Table 3.

3. Pre-policy calibration

This section will show that the SE(A+O)R model with the parametric restriction $\gamma^A = \gamma^O := \gamma$ provides a good fit to observations of the early pandemic for countries such as Canada and Italy, when calibrated to fit the confirmed daily new case data for the period $[T_1, T_2 + 5]$ (i.e. the pre-policy period plus 5 days).

3.1. Measurements and observations

The ODE system (1) captures the dynamics of the unobserved state of the population, and should be supplemented by assumptions about how the system is observed:

Assumptions 2. *During the pre-policy period $[T_0, T_2]$, model parameters are constant. Among the OC population, an expected fraction φ^O are counted as confirmed cases, typically as a result of either a positive RT-PCR test ("swab test") or a diagnosis by symptoms. In contrast, none of the AC population are counted as confirmed cases ($\varphi^A = 0$).*

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Let us denote the confirmed daily new cases on the day ending at time $T_1 + k$ by $\hat{\text{DNC}}_k$, for $k = 1, 2, \ldots, K = T_2 + 5 - T_1$. We make the assumption that the data generating process is a random process fluctuating around $X_+(t)$, the dominant solution (9) of the linearized SEAOR model:

$$\widehat{\text{DNC}}_k = \left(\varphi^O (1-r)\beta \int_{T_1+k-1}^{T_1+k} E(s)ds \right) e^{\zeta_k}. \tag{11}$$

Here $E(s) = E_0 e^{\lambda_+(s-T_1)}$ with $E_0 = E(T_1)$, and λ_+ is given by (6).

3.3. Pre-policy calibration: Italy and Canada

As long as the number of new cases is not too small, it is reasonable to assume $(\zeta_k)_{k=1,2,\ldots,K}$ in (11) is an i.i.d. $N(0, \sigma^2)$ sequence of residuals, which leads to a simple linear regression:

Table 3
The pre-policy and post-policy periods in Italy and Canada extend over $[T_1, T_2]$ and $[T_2, T_3]$ respectively, where T_1, T_2 are shown in the table and $T_3 = T_2 + 42$, which is six weeks after policy time.

Country	Pandemic Time (T_1)	Policy Time (T_2)
Italy	$T_1 = 52$ (start of February 22, 79 Cases)	$T_2 = 68$ (start of March 10, Nationwide lockdown)
Canada	$T_1 = 48$ (start of February 18, 51 Cases)	$T_2 = 73$ (start of March 15, Ontario School Shutdown)

$$\log \widehat{\mathrm{DNC}}_k = \kappa + \lambda_+ k + \zeta_k, \quad k = 1, 2, \ldots, K$$

with mean-squared error

$$\hat{\sigma}^2 = \mathrm{MSE}_K = \frac{1}{K} \sum_{k=1}^{K} |\log(\widehat{\mathrm{DNC}}_k) - \kappa - \lambda_+ k|^2 \tag{12}$$

and $\kappa := \log(\varphi^O(1-r)\beta E_0(1-e^{-\lambda_+})/\lambda_+)$. We then obtain least square estimates for the two identifiable parameters, $\hat{\theta} = (\hat{\kappa}, \hat{\lambda}_+)$. Table 4 shows the parameter values resulting from the calibrations for Canada and Italy, including important parameters $\hat{\alpha}^{\mathrm{eff}}, \hat{\lambda}_-, \hat{\nu}_+, R_0$ as determined by (6). Fig. 1 displays values given by the calibrated models and observed data for daily new cases on a log-scale. These figures show that for both Italy and Canada, the calibrated model gives a good fit, albeit with a significant degree of noise due to the small number of confirmed cases.

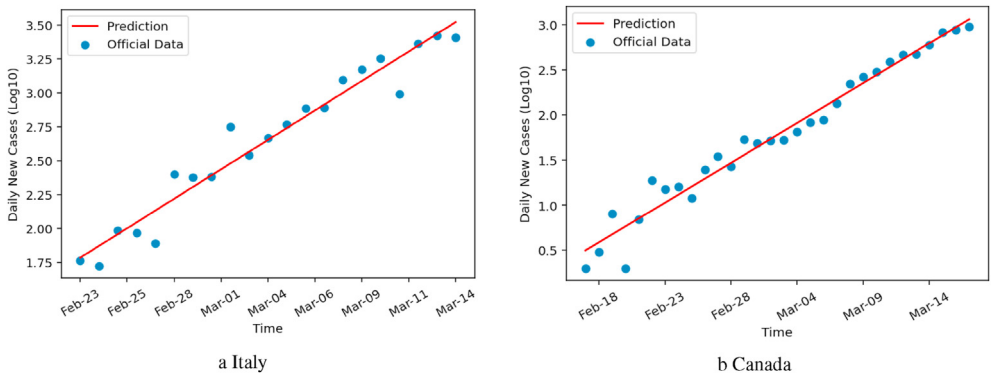
These parameter estimates do not fully determine the model and its initial conditions: r, φ^O, α^O, α^A, E_0 are not separately identifiable, but are constrained by two equations:

$$\hat{\kappa} = \log(\beta\varphi^O(1-r)E_0(1-e^{-\hat{\lambda}_+}) \Big/ \hat{\lambda}_+), \quad \hat{\alpha}^{\mathrm{eff}} = (1-r)\alpha^O + r\alpha^A \tag{13}$$

Table 5 provides the best-fit values for the actual state (as opposed to the observed state) of the pandemic on the dates T_1, T_2 using the linearized solutions

Table 4
Parameter estimates for Italy and Canada during the pre-policy period.

Country	$\hat{\kappa}$	$\hat{\lambda}_+$	MSE $= \hat{\sigma}^2$	$\hat{\lambda}_-$	$\hat{\alpha}^{\mathrm{eff}}$	$\hat{\nu}_+$	R_0
Italy	1.6974	0.1999	0.015	−0.5666	1.214e-08	0.546	4.40
Canada	0.4090	0.2037	0.021	−0.5703	1.988e-08	0.540	4.48



a Italy b Canada

Fig. 1. Simulation and official data of daily new cases (DNC) for Italy and Canada in the pre-policy calibration period $[T_1, T_2 + 5]$.

Table 5
The actual state of the pandemic in Italy and Canada at times T_1, T_2, obtained by calibrating the linearized model to daily new case data and depending on the additional parameters φ^O, r. Given r, the actual asymptomatic and ordinary carrier populations will be $A(t) = rI(t)$, $O(t) = (1-r)I(t)$. Note: the table has also been computed for the non-linear model and found to yield values of $E(T_2)$ and $I(T_2)$ that differ from this table by not more than 2.5%.

$\varphi^O(1-r)$	Country	$E(T_1)$	$I(T_1)$	$R(T_1)$	$E(T_2)$	$I(T_2)$	$R(T_2)$
20%	Italy	150	82	68	8208	4478	3731
	Canada	41	22	18	15279	8251	5609
40%	Italy	75	41	34	4104	2239	1865
	Canada	20	11	9	7639	4125	2804
60%	Italy	50	27	22	2736	1492	1243
	Canada	13	7	6	5093	2750	1869
80%	Italy	37	20	17	2052	1119	932
	Canada	10	5	4	3819	2062	1402
100%	Italy	30	16	13	1641	895	746
	Canada	8	4	3	3055	1650	1121

$$E(t) = \left(\beta\varphi^O(1-r)\left(1-e^{-\hat{\lambda}_+)/\hat{\lambda}_+}\right)^{-1}e^{\hat{\kappa}+\hat{\lambda}_+(t-T_1)} \tag{14}$$

$$I(t) = \hat{v}_+\left(\beta\varphi^O(1-r)\left(1-e^{-\hat{\lambda}_+)/\hat{\lambda}_+}\right)^{-1}e^{\hat{\kappa}+\hat{\lambda}_+(t-T_1)} \tag{15}$$

assuming the model may have different values of $\varphi^O(1-r)$. The removed value $R(t)$ can be accurately approximated by $\gamma\int_{-\infty}^{t} I(s)\,ds = \gamma I(t)/\hat{\lambda}_+$. Although not shown here, the linear approximation of (1) underlying Table 5 has been validated: The solutions of the full non-linear system starting from the specified initial conditions at time T_1 have been also been computed and found to yield values of $E(T_2)$ and $I(T_2)$ that differ by not more than 2.5% from those shown in the Table.

Finally, we note that to determine the separated compartment populations $A(t) = rI(t)$, $O(t) = (1-r)I(t)$, the value of r is also needed. As we will find in the next section, this indistinguishability of models leads to difficulty about the efficacy of different health policy interventions.

4. Public health policy interventions

Policy makers seek to control the disease by taking actions that reduce the transmission parameters α^O, α^A, thereby decreasing the exposure rate of the susceptible population to viral carriers. Other important parameters, notably β, γ, r, are not controllable and remain unchanged by such policies. In this section, we formalize how the effectiveness of general policies can be analyzed in terms of their impact on R_0. These ideas will be illustrated with the example of Italy under a range of hypothetical scenarios where a substantial health policy intervention is made instantaneously on the policy date T_2, with a constant level of effort thereafter.

4.1. Policy choices

To quantify the effect of policy type p, we first define the *maximal effect* of p, the result of implementing p with the largest feasible effort, to act on (α^O, α^A) leading to new values $(1-v_p^O)\alpha^O, (1-v_p^A)\alpha^A$, where $(v_p^O, v_p^A)\in[0,1]^2$ is called the *maximal effect vector* of p. More generally, the policy p applied with a *partial effort* $e_p \in [0,1]$ is defined by the action

$$(\alpha^O, \alpha^A) \to (\alpha_p^O, \alpha_p^A) = \left((1-e_p v_p^O)\alpha^O, (1-e_p v_p^A)\alpha^A\right). \tag{16}$$

This Definition, apparently new, formalizes notions of policy efficacy commonly found in the literature. It distinguishes the type of policy (encoded by the vector (v_p^O, v_p^A)) from e_p, the degree of effort applied to that policy. Such actions have a direct effect on the basic reproduction number R_0:

Proposition 3. *Let* $\zeta = \frac{r\alpha^A}{(1-r)\alpha^O + r\alpha^A}$ *and assume* $\gamma^A = \gamma^O = \gamma$. *Then the change in* R_0 *under the policy given by* (16) *is*

$$R_0 \to R_{0p} = [1 - e_p((1-\zeta)v_p^O + \zeta v_p^A)]R_0 \tag{17}$$

and thus the efficacy of the policy is $e_p((1-\zeta)v_p^O + \zeta v_p^A)$.

Proof. By (7), $R_0 = \frac{\alpha^{\text{eff}}N}{\gamma}$. Since $r\alpha^A = \zeta\alpha^{\text{eff}}$ and $(1-r)\alpha^O = (1-\zeta)\alpha^{\text{eff}}$, under (16) one finds

$$R_{0p} = \frac{((1-r)\alpha_p^O + r\alpha_p^A)N}{\gamma} = [(1-\zeta)(1-e_p v_p^O) + \zeta(1-e_p v_p^A)]\frac{\alpha^{\text{eff}}N}{\gamma} = [1 - e_p((1-\zeta)v_p^O + \zeta v_p^A)]R_0.$$

Remarks 3. *There is an important policy message to be drawn from this simple result. Compared to the equivalent model with* $r = 0$ *the efficacy of any policy that leaves* α^A *unchanged is reduced by the factor* $\zeta = (1 + r(\rho - 1))^{-1}r\rho$, *which is increasingly dependent on the unobserved parameter* r *as* ρ *increases.*

The following types of policy have been implemented with varying degrees of effort in a wide range of countries during the early pandemic.

1. **Isolation of Infective Patients:** This type of policy ($p = 1$) prevents actively infectious cases from encountering susceptible people, and directly targets the close contact parameter z^O. We suppose that the maximal effect on any one confirmed carrier is to reduce their close contact rate by a fraction f; asymptomatic people and unconfirmed ordinary carriers are not affected. Thus the maximal effect vector of this policy is $v_1 = (f\varphi^O, 0)$, and with effort e_1 its effect on the transmission parameters is

$$(\alpha^O, \alpha^A) \to (\alpha_1^O, \alpha_1^A) = \left((1 - e_1 f \varphi^O)\alpha^O, \alpha^A\right). \tag{18}$$

Contact tracing is a policy that improves the effectiveness of isolation by identifying a larger fraction of infectious cases. It seeks both to increase the parameter $\varphi^O > \varphi$, and to identify a fraction $\varphi^A > 0$ of asymptomatic cases. All these additional cases would then be included in the implementation of isolation policy. Effectively then, isolation combined with improved contact tracing has a maximal vector $(\nu_1^O, \nu_1^A) = (f\varphi^O, f\varphi^A)$.

2. **Social Distancing:** Social distancing ($p = 2$), such as a policy that requires keeping at least 2m distance in public spaces, can be targeted at identifiable sub-populations, or applied fairly across the general population. A strategy that targets the general population fairly will have equal impact on the close contact fractions z^O, z^A for both ordinary and asymptomatic carriers. If implemented with effort e_2 and maximal effect vector (ν_2, ν_2), the policy leads to

$$(\alpha^O, \alpha^A) \to (\alpha_2^O, \alpha_2^A) = \left((1 - e_2\nu_2)\alpha^O, (1 - e_2\nu_2)\alpha^A\right). \tag{19}$$

3. **Protective Garments:** The wearing of personal protective equipment (PPE) ($p = 3$), including gloves, gowns, masks, face shields and eye protection reduces the transmission probabilities τ^O, τ^A. If applied to the general population with effort e_3 and a maximal effect vector (ν_3, ν_3), this policy leads to

$$(\alpha^O, \alpha^A) \to (\alpha_3^O, \alpha_3^A) = \left((1 - e_3\nu_3)\alpha^O, (1 - e_3\nu_3)\alpha^A\right). \tag{20}$$

Some studies are helpful for determining ν: For example, Li et al., (2006) claim that the efficiency of surgical masks is 95%, compared with 97% for N95 masks.

4. **Hygiene:** Infection via contaminated "fomites" (i.e. inanimate surfaces or objects), where active virus is absorbed from surfaces, has been considered an important mode of COVID transmission. Cleanliness ($p = 4$), particularly frequent handwashing and disinfecting surfaces, is the most important way of reducing spreading by viral contamination of fomites. If implemented across the general population with effort e and maximal effect vector (ν_4, ν_4), a cleanliness policy has the following effect

$$(\alpha^O, \alpha^A) \to (\alpha_4^O, \alpha_4^A) = \left((1 - e_4\nu_4)\alpha^O, (1 - e_4\nu_4)\alpha^A\right). \tag{21}$$

Recent studies summarized in Mondelli et al., (2021) have cast doubt on the overall importance of fomite transmission compared to aerosol transmission, which suggests that ν_4 is small.

Remarks 4. *A vaccine is potentially the most powerful intervention tool. It acts directly on the immune system of susceptible individuals to substantially reduce the infection probability τ, and indirectly in reducing the infectiousness of vaccinated carriers. We do not consider vaccination further because it was not available early in the pandemic. Moreover, the SE(A+O)R framework is inadequate to address vaccination, and an alternative approach should be followed that extends the number of compartments in the model, see for example Arino et al. (2008).*

Let us now take the point of view of the Italian National Health Authority that recognized the potentially devastating impact of the pandemic, and implemented a remediation strategy effective at the policy time T_2, March 10, 2020. The best data available at that time indicates that the pandemic has a daily exponential growth rate $\lambda_+ \sim 0.1999$, and an effective reproduction number $R_0 \sim 4.40$. To bring the pandemic under control will therefore require extreme measures: we suppose the authority aims to reduce R_0 to a value less than 0.8, ensuring a reasonably quick resolution of the breakout. They may choose from the above policies labeled by p, either one at a time with varying efforts, or in combinations.

Table 6 provides our benchmark parameter values in the context of policy interventions early in the pandemic in Italy. These values have been chosen for expository purposes to illustrate the uncertainties due to r. They are not intended to be realistic: the choice of realistic values is deserving of further study. Most of our main conclusions will be qualitatively similar under moderate changes to the benchmark parameters.

Table 6
Benchmark parameters for Italy for the four single policies. The assumed values of other parameters are: $\varphi = 90\%$, $\rho = \alpha^A/\alpha^O = 4$ and r is variable. Recall the pre-policy value $R_0 \sim 4.4$ for Italy from Table 4.

	$p = 1$	$p = 2$ Social	$p = 3$ Protective	$p = 4$
	Isolation	Distancing	Garments	Hygiene
ν_p^O	$f\varphi = (0.9)(0.9)$	0.7	0.85	0.1
ν_p^A	0	0.7	0.85	0.1
e_p	1	0.7	0.95	0.5
α_p^O/α^O	0.19	0.51	0.19	0.95
α_p^A/α^A	1	0.51	0.19	0.95
R_{0p}/R_0	r dependent	0.51	0.19	0.95

4.2. Single strategies

In this section, we use the calibrated base model for Italy to analyze the effect of implementing a single strategy, taking the benchmark policy parameters from Table 6. We focus on two distinct policy strategies, implemented singly: (a) isolation of all confirmed symptomatic patients (strategy $p = 1$), (b) protective garments for the general population (strategy $p = 3$). Our primary focus is on the effect of these policies for a range of values [0, 60%] of the asymptomatic rate r. We will demonstrate the important point that the effectiveness of a policy that applies equally to the entire population, as in case (b), does not depend on r, while in contrast, the effectiveness of a policy that targets only confirmed active cases, such as isolation, can not be predicted without knowing r.

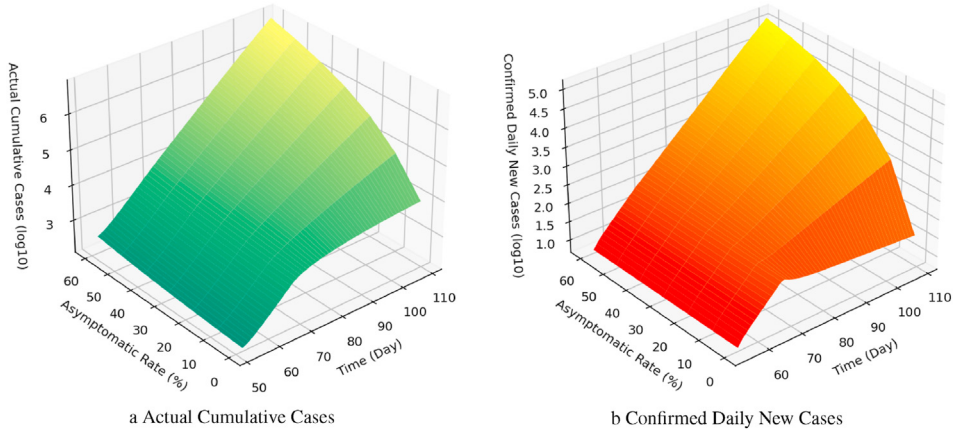
4.2.1. Effectiveness of isolation

Let us suppose that when isolation is maximally implemented, the average transmission rate for confirmed cases is reduced by $f = 90\%$ in Eq (18). By Proposition 3, the overall effectiveness on the disease itself is determined by the ratio $R_{01}/R_0 = 1 - (1 - \zeta)f\varphi$, which if $\zeta = 0$ yields the favourable result $R_{01} = (0.19) \times 4.4 \sim 0.84$. Fig. 2 shows the logarithm of the actual cumulative cases and confirmed daily new cases predicted by the model for Italy during the entire pre-post period $[T_1, T_3]$, under the maximal isolation policy, when $\rho = \alpha^A/\alpha^O = 4$. With these parameters, what appears to be a strong policy measure will fail outright with $R_{01} > 1$ if the asymptomatic rate r exceeds about 1.2% if $\rho = 4$ (or $r > 2.6\%$ if $\rho = 2$). Of course the results will be even worse if the effort parameter is $e < 1$.

4.2.2. Effectiveness of protective garments

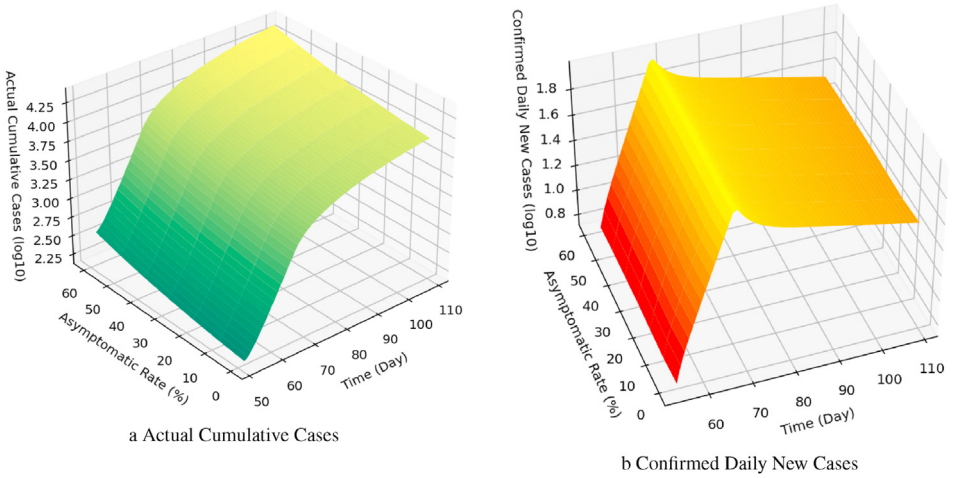
Here we consider the effect of a nation-wide policy of mask wearing where for definiteness we suppose there is a maximal effect $\nu_3 := \nu_3^O = \nu_3^A = 0.85$, and a degree of effort $e_3 = 0.95$. In this setting, the result does not depend on r or ρ. Fig. 3 shows the logarithm of the actual cumulative cases and confirmed daily new cases predicted by the model for Italy during the entire pre-post period $[T_1, T_3]$, under the mask wearing policy. By Proposition 3, we see that under all variations of the model with $\nu_3 = 0.85$, $e_3 = 0.95$ the pandemic is brought under control, with $R_{03} \sim 0.1925 \times R_0 \sim 0.847$.

Fig. 4 shows how isolation and mask wearing policies lead to very different outcomes for the pandemic. Under some reasonable assumptions on r, φ and ρ the maximal isolation policy has very little impact on the pandemic, while the protective garments policy is able to eliminate the disease if implemented with maximal effort.



a Actual Cumulative Cases b Confirmed Daily New Cases

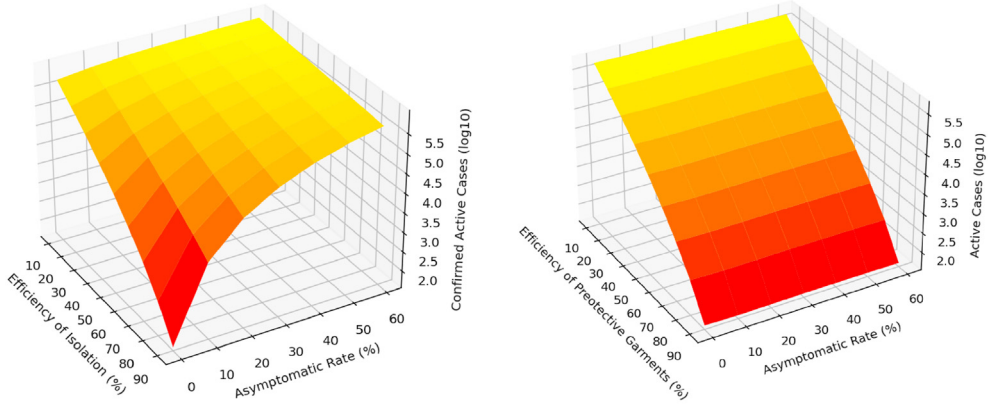
Fig. 2. ITALY: The model prediction showing the effect of the maximal isolation policy if implemented at the policy time T_2 (March 10, 2020). Here we fix the pre-policy ratio $\rho = \alpha^A/\alpha^O = 4$, the transmission reduction factor $f = 0.9$ and the confirmation factor $\varphi^O = 0.9$, and plot over the period $[T_1, T_3]$ for varying r. The first graph shows the logarithm of the actual cumulative cases consisting of all symptomatic and asymptomatic infections plus removed cases. The second graph shows the logarithm of the confirmed daily new cases.



a Actual Cumulative Cases

b Confirmed Daily New Cases

Fig. 3. ITALY: The model prediction showing the effect of the maximally protective garments if implemented at the policy time T_2 (March 10, 2020). Here we fix the policy factors $v_3 = 0.85$, $e_3 = 0.95$, and show that the pandemic curve over the period $[T_1, T_3]$ is independent of r. These graphs are independent of ρ. The first graph shows the logarithm of the actual cumulative cases consisting of all symptomatic and asymptomatic infections plus removed patients. The second graph shows the logarithm of the confirmed daily new cases.



a Isolation

b Protective Garments

Fig. 4. The effect of isolation and protective garments compared: These graphs show the logarithm of the active confirmed cases in Italy at time T_3 corresponding to April 20, 2020. The left graph shows the dependence on the effort expended on isolation, $v_1e_1 \in [0, 1]$, and on the asymptomatic rate $r \in [0, 0.6]$. The right graph shows the dependence on the effort expended on protective garments, $v_3e_3 \in [0, 1]$, and on the asymptomatic rate $r \in [0, 0.6]$ when $\varphi = 1$ and $\rho = 4$.

When the general population adopts social distancing (strategy $p = 2$), the effect is similar to the protective garment policy in that α^A, α^O are changed by equal fractions, (v_2, v_2), even though it targets z^A, z^O instead of τ^A, τ^O. Similarly, improved hygiene (strategy $p = 4$) leads to equal fractions (v_4, v_4). In the next section, we combine these three strategies into a single policy we call *General Personal Protection*, and use the logic of the previous analysis for protective garments.

4.3. Combining public health policies

We have seen that for Italy, standard epidemic management policy, which is to expend maximal effort $e_1 = 1$ to identify and isolate all known active covid cases, fails to contain the crisis if $r > 1.2\%$ and $\rho = 4$. We now consider how the full set of COVID mitigation strategies $p \in \mathbf{P}$ can be implemented in combination, following the "swiss cheese" metaphor. First note that some care is needed to account for possible interference between the effects of different strategies. Under the following assumption, such interference effects have been eliminated through the design of the policy:

Assumption 4. *[Independent policy assumption] The effect of the set of strategies $p \not\equiv \boldsymbol{P}$ when implemented in combination with efforts $e = (e_p)_{p\in\mathbf{P}} \in [0, 1]^{\mathbf{P}}$ is to map the transmission parameters to new values:*

$$(\alpha^O, \alpha^A) \to \left(\alpha^O \prod_{p \in \mathbf{P}} (1 - e_p \nu_p^O), \alpha^A \prod_{p \in \mathbf{P}} (1 - e_p \nu_p^A) \right). \tag{22}$$

The three policies $p = 2, 3, 4$, thought of as social distancing (including shutting down some businesses and enforcing distancing rules), mask wearing and improved hygiene (including widespread use of hand sanitizer), when applied equally across the general population, have a similar impact on R_0. They can therefore be combined into one policy which we call *general personal protection* (GPP). Following (22), their collective maximal and partial effects when implemented with efforts (e_2, e_3, e_4), will be equal multiplicative factors on both α^O, α^A:

$$(1 - \nu_{\text{GPP}}) := \Pi_{p \in \{2,3,4\}} (1 - \nu_p), \quad (1 - e_{\text{GPP}} \nu_{\text{GPP}}) := \Pi_{p \in \{2,3,4\}} (1 - e_p \nu_p). \tag{23}$$

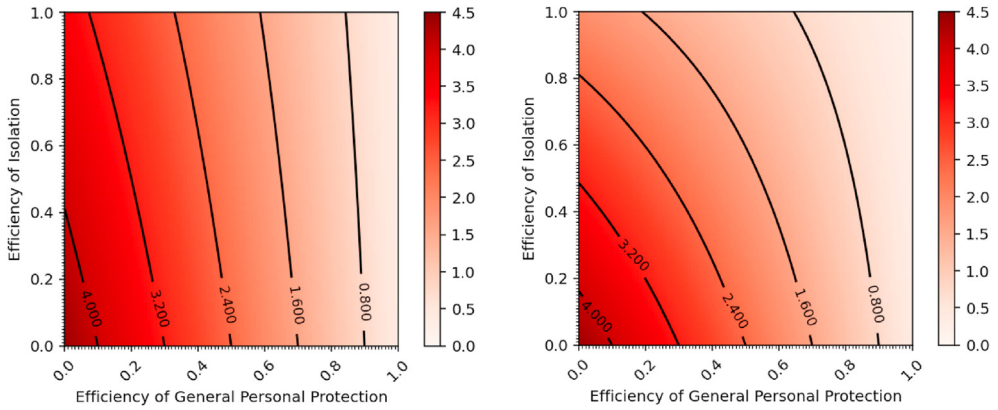
The benchmark parameter values shown in Table 6 lead to the maximal collective effect $\nu_{\text{GPP}} = 0.91$, which is of course better than can be achieved by any single policy.

Fig. 5 shows contour plots of the achieved value of R_0 under a combination of isolation with GPP for variable levels of e_1, e_{GPP} when $\nu_1 = 0.81$, $\nu_{\text{GPP}} = 0.91$. The first assumes $r = 40\%$; the second assumes $r = 10\%$; both assume $\rho = 4$. We see clearly from this that if $r = 40\%$, achieving the desired value $R_{0p} = 0.8$ requires a far greater effort than the hypothetical proposed strategy. When $r = 40\%$, only a combination of GPP with $e_{\text{GPP}} = 90\%$ effort and maximal isolation policy can control the pandemic. A strict isolation policy ($e_1 = 100\%$) combined with GPP with $e_{\text{GPP}} = 70\%$ effort that seems sufficient to achieve $R_{0p} = 0.8$ if the authority mistakenly assumes $r = 10\%$, only achieves $R_{0p} = 1.4$ if it turns out that $r = 40\%$.

5. Discussion and conclusions

We have chosen the simplest possible model, the SE(A+O)R model, to demonstrate the sensitivity of policy to the presence of asymptomatic carriers. Perhaps the single most striking result of this paper is the high sensitivity of standard isolation policy outcomes to the value of r. The analysis underlying Fig. 2, in particular Proposition 3, combined with illustrative parameter choices, shows that a plausible COVID-19 intervention for Italy with 81% efficacy and achieving $R_{0p} = 0.84$ if $r = 0$, leads to efficacy $< 77\%$ and policy failure with $R_{0p} > 1$ if r as small as 1.2%. If r is as high as 40%, the policy has very little impact, and leads to only a slight reduction from $R_0 = 4.40$ to $R_{0p} = 3.89$. At the same time, we also show that policies such as social distancing and mask wearing that apply to the general population are insensitive to r. In this way, our simple model might persuade reluctant politicians that without paying the high social cost of population-wide policies a pandemic that spreads asymptomatically may not be contained.

As Flaxman et al., (2020) show, most European countries applied a succession of policies during March 2020 culminating in a "complete lockdown" that corresponds to a maximal policy of social distancing. This pattern reflects that the earlier interventions, notably standard isolation, were not effective enough, a mistake that might have been avoided had asymptomatic carriers been anticipated. Our paper provides a concise general methodology for quantifying outcomes of any such combinations of policies, with Proposition 3 giving a clear formula for the value of the resultant R_{0p} in terms of the underlying parameters.



a R_{0p} with two policies if $r = 40\%$. b R_{0p} with two policies if $r = 10\%$.

Fig. 5. This plot shows the effective R_{0p} after policy date T_2 in Italy as a function of e_1, e_{GPP}, when isolation is applied with effort e_1 and $\nu_1 = 0.8$, and general personal protection is applied with effort e_{GPP} and $\nu_{\text{GPP}} = 0.91$. The darkness of the red colour denotes the value of R_{0p}. Plot (a) shows results when $r = 40\%$, (b) assumes $r = 10\%$; both plots have $\rho = 4$.

Two of the apparent mathematical limitations of our analysis are easily overcome. Proposition 2 allowed us to focus on constant ratio solutions with $A(t)$: $O(t) = r$: $(1 - r)$, that are stable attractors of more general solutions of the non-linear system. This proposition, including the formula $\alpha^{\text{eff}}(t) = (1 - r)\alpha^{O}(t) + r\alpha^{A}(t)$, continues to hold in more general models with time-varying parameters and more complex compartment structures, provided the parametric restriction $\gamma^{A} = \gamma^{O}$ is correctly generalized. Our main qualitative conclusions about policy indeterminacy will continue to hold in a wide range of models that more adequately reflect real world complexity. Secondly, the linearized analysis of Section 2.4 about the disease-free state, and consequently Proposition 3, can be extended to linearizations about the disease state at any time, in more general models, leading to similar formulas that predict policy efficacy over any short period of time, for example, when a disease is endemic.

The ad hoc values we assigned to poorly understood parameters and displayed in Table 6, especially the ratio $\rho = \alpha^{A}/\alpha^{O}$, were chosen for expository purposes. This is not a limitation: The formulas we derive in this paper provide simple tools for any researcher to explore the sensitivity of policy outcomes to changes in these parameter values. Our conclusions strongly suggest that efforts to pin down reliable values will be rewarded by improved projections in a host of what-if studies on the effects of policy interventions. Pinning down the most critical parameter, r, requires large scale random testing of the general population as well as systematic testing of close contacts, which is very difficult for an emergent infectious disease. However, since the existence of asymptomatic carriers is not an unexpected characteristic of infectious diseases, managing any future emergent disease may fail catastrophically unless a strong early effort is made to determine r.

Declaration of competing interest

None.

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