



BANCA D'ITALIA
EUROSISTEMA

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containment measures

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AN EPIDEMIC MODEL FOR SARS-COV-2 WITH SELF-ADAPTIVE CONTAINMENT MEASURES

by S. Marchetti^a, A. Borin^a, F. P. Conteduca^a, G. Ilardi^b, G. Guzzetta^c, P. Poletti^c, P. Pezzotti^d, A. Bella^d, P. Stefanelli^d, F. Riccardo^d, S. Merler^c, A. Brandolini^a and S. Brusaferro^e

Abstract

During the Covid-19 pandemic, several countries have resorted to self-adaptive mechanisms that allow non-pharmaceutical interventions to be tailored to local epidemiological and health care indicators. These mechanisms reinforce the interdependence between containment measures and the evolution of the epidemic, mostly overlooked by existing epidemiological models. In our innovative approach, we instead develop a model that embeds an algorithm mimicking the self-adaptive policy mechanism, effective in Italy since November 2020, and allows us to track the historical evolution of both health outcomes and restrictions in the country. By focusing on the epidemic wave triggered by the onset of the Delta variant, we compare the functioning of alternative mechanisms to show how the policy framework may affect the trade-off between health outcomes and the restrictiveness of mitigation measures. This trade-off varies considerably depending on specific conditions (e.g. vaccination coverage), with less reactive mechanisms (e.g. those based on occupancy rates) becoming more advantageous in favourable contexts.

JEL Classification: H51, I12, I18.

Keywords: Covid-19, epidemiological model, restrictions, Italy.

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1 Introduction¹

During the Covid-19 pandemic, public authorities faced the demanding task of adopting mitigation policies to minimise the strain on health systems while considering the socio-economic costs associated with them. At the onset of the pandemic in spring 2020, several countries resorted to nationwide lockdowns, also given the high uncertainty about the impact of the novel disease on the national health systems. The effects of these policies have been profound both for public health [28, 34, 63, 57, 17, 22] and socio-economic variables worldwide [16, 18, 31, 11, 30, 46, 8, 19]. After the initial emergency, a new surge in cases in autumn 2020 prompted many countries to introduce tier systems of contingent measures based on epidemiological indicators such as incidence and growth rates of confirmed cases and hospital bed occupancy rates (e.g., Germany [36], the United Kingdom [75], and France [66]). Unlike the initial lockdowns, these mechanisms allow for a dynamic adaptation of non-pharmaceutical interventions (NPIs) to the evolution of the epidemic. Compared with purely discretionary measures, such rule-based systems offer several advantages, including predictability and time-consistency of the responses and geographical differentiation of the interventions within a common nationwide approach.

Analyses, often supported by an underlying epidemiological model, generally focus on the role of specific policy interventions (e.g., border closure [73], mask mandate [1, 33], remote working [3], vaccination [59], school closures [77, 7, 51, 69]). In particular, introducing a particular policy impacts the epidemic's evolution everything else fixed. While still valid, such an approach overlooks the critical interplay between the epidemic trajectory and response mitigation policies observed in the real world. In other words, governments tend to calibrate their policies and containment measures depending on the epidemiological situation and its evolution following the enforced interventions. This aspect becomes even more relevant with rule-based mechanisms in which the epidemic and restrictions interact almost automatically. In this case, designing specific modeling tools is critical to studying and evaluating possible epidemic trajectories under different self-adaptive mechanisms and

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informing the decision process of a policymaker aiming to select a policy that meets her objectives in terms of health and social interaction outcomes.

This paper presents an epidemiological model for Covid-19, embedding four alternative policy-response mechanisms, three of which enforced in Italy after November 2020. The first one (*Rt-New Positives*), in place from March 2021 to May 2021, is mainly based on the reproduction number, Rt - i.e. the expected number of secondary cases per infectious individual at a given time t - estimated on reported symptomatic cases and the weekly incidence. The latter is primarily used by the second mechanism (*Incidence*), in force from May to July 2021. The third mechanism (*Occupancy rates*), effective since July 2021, considers occupancy rates of non-critical medical area (MA) and intensive care unit (ICU) beds as leading indicators (see Methods and Supplementary information). On top of actually implemented schemes, we also design an additional mechanism that might be interesting from a policy perspective. The mechanism takes the reproduction number estimated on hospital admissions in MA (*Rt-Hospital admissions*) as the main policy indicator. As compared to the *Rt-New positives mechanism*, this alternative scheme may accommodate the decoupling between the evolution of new cases and that of hospital admissions induced by the high and long-lasting vaccine protection against the severe disease have generated. Furthermore, the possibility of introducing a newly designed mechanism proves the flexibility of our approach.

Following the weekly collection of epidemic indicators carried out by the Italian Ministry of Health (MoH), the policy mechanism defines the tier-based restrictions through an algorithm depending on the value of the indicators themselves. In particular, the MoH assigns each Italian region to a zone of containment measures (white, with mild restrictions, yellow, orange, or red, with near-lockdown provisions). Although the Italian government adjusted the rule-based mechanism over time to accommodate changes in the epidemiological setting (e.g., the onset of new variants, the progressive achievement of high vaccination coverage), the provisions within each tier have been mostly consistent over time, at least for unvaccinated individuals. The four mechanisms are evaluated in terms of critical epidemiological indicators, like the number of daily new cases, occupancy rates in MAs and ICUs, and the Italy Stringency index [20], an *ad hoc* synthetic indicator measuring the intensity of restrictions implemented in Italy throughout the pandemic and which stems from the Oxford Stringency Index [32].

1.1 Related Work

A thorough understanding of the feedback between health outcomes and economic activity proved crucial for policy-makers, to assess the extent to which the impact of the economic-wide pandemic would distribute within a country. In most cases, fully-fledged macroeconomic tools have been used to investigate the effects of pandemic-related outliers on macroeconomic indicators (e.g., [48, 9, 15, 27]) or to explore the spillovers on trade and production networks [14]. Our paper contributes to the literature on SIR-macro models, enabling macroeconomic impact assessment of alternative policy measures within a coherent analytical framework [10, 25, 2, 56]. In detail, we integrate an extended SIR model with an algorithmic component enhancing self-adaptive adjustment of the infection rate levels based on epidemic outcomes. Remarkably, the embedded algorithmic component mimics the actual policy mechanism adopted by the Italian government. On a weekly basis, rule-based evaluation of epidemiological indicators enforces adaptive NPIs on a regional basis, to balance the health-wealth trade-off posed by the Covid-19 pandemic [21]. To enable derivation of the epidemiological indicators required for the functioning of the policy mechanism, we extend the SIR model and account for several transition paths of individuals across states, allowing for geographic and demographic heterogeneity of the Italian population. Other works by national and international policy institutions featured a static policy-oriented component and a SIR model to address such task [5, 12, 71]. Our contribution is the first to track the interplay between epidemiological dynamics and economic activity in a fully comprehensive framework to the best of our knowledge.

2 Results

This section shows how our approach may provide illustrative scenarios for the evolution of the Covid-19 epidemic. We assess and compare the impact of different mechanisms of self-adaptive interventions on health and social-interaction outcomes.

The core of our framework is the interaction between the SARS-CoV-2 transmission, modelled with an extended SIR model [47], and restrictions, introduced through an algorithmic component that replicates the mechanism implemented in Italy since November 2020. We test the impact of alterna-

tive self-adaptive rule-based mechanisms in the presence of the Delta variant under different hypotheses on the vaccine rollout during the simulation period (July 2021-March 2022). However, we abstract from the emergence of the Omicron variant in December 2021 since it would make the comparison among the mechanisms less compelling. Further details Section Methods are provided in the Section Methods and in the Supplementary Information.

Tab. 1 summarises the main results for the different policy mechanisms and vaccination scenarios. Fig. 1 shows the evolution of the target variables obtained under the baseline (historical) vaccination campaign (*Actual rollout*). Under all mechanisms, epidemic variables are characterised by two waves as in the historical data. The summertime wave is attributable to the onset of the Delta variant, whose spread was boosted by the increased mobility observed throughout the first decade of July, in coincidence with the European Football Championship. The fall-winter wave was driven by several factors, possibly including the waning efficacy of the vaccines and the increase in indoor social interactions associated with lower temperatures, school re-openings, and a substantial return to workplaces. However, some relevant differences across the mechanisms emerge.

| Vaccine Rollout | Policy Mechanism | New Positives per day | Average MA Occupancy Rate | Average ICU Occupancy Rate | Stringency Index (ItSI, average) |
|--------------------|------------------|-----------------------|---------------------------|----------------------------|----------------------------------|
| <i>Actual</i> | Rt-New positives | 2384 [2187, 2965] | 3.6% [3.5%, 4.0%] | 2.0% [1.9%, 2.5%] | 34.3 [33.6, 35.6] |
| | Incidence | 3836 [3327, 5463] | 5.2% [4.7%, 6.6%] | 3.3% [2.8%, 4.8%] | 28.0 [26.8, 29.8] |
| | Occupancy rates | 7175 [6331, 8417] | 7.8% [7.1%, 8.8%] | 5.4% [4.7%, 6.6%] | 23.9 [22.7, 26.3] |
| <i>Optimistic</i> | Rt-Hospital adm. | 3061 [2748, 3717] | 4.5% [4.2%, 5.1%] | 2.7% [2.4%, 3.3%] | 31.2 [29.9, 34.1] |
| | Rt-New positives | 2074 [1830, 2202] | 3.1% [2.9%, 3.2%] | 1.7% [1.6%, 1.9%] | 29.2 [26.9, 33.4] |
| | Incidence | 2809 [2380, 3674] | 3.9% [3.6%, 4.6%] | 2.4% [2.0%, 3.1%] | 24.9 [22.9, 26.9] |
| <i>Pessimistic</i> | Occupancy rates | 4629 [3315, 6405] | 5.3% [4.4%, 6.7%] | 3.5% [2.6%, 4.8%] | 20.8 [20.3, 22.9] |
| | Rt-Hospital adm. | 2335 [2071, 2811] | 3.5% [3.3%, 3.9%] | 2.0% [1.8%, 2.5%] | 28.0 [25.5, 30.0] |
| | Rt-New positives | 3156 [2808, 3837] | 4.5% [4.2%, 5.0%] | 2.5% [2.3%, 3.1%] | 36.4 [35.0, 39.6] |
| | Incidence | 5327 [4625, 7305] | 6.9% [6.3%, 8.4%] | 4.4% [3.7%, 5.9%] | 30.7 [29.1, 32.0] |
| | Occupancy rates | 9177 [8553, 10416] | 9.8% [9.3%, 10.8%] | 6.6% [6.0%, 7.9%] | 26.0 [25.2, 28.2] |
| | Rt-Hospital adm. | 3878 [3558, 4538] | 5.5% [5.2%, 6.3%] | 3.3% [2.9%, 3.9%] | 34.8 [32.4, 39.0] |

Table 1: Average values of new positives, MA occupancy rate, ICU occupancy rate, and the ItSI under each mechanism (*Rt-New positives*, *Incidence*, *Occupancy rates*, *Rt-Hospital admissions*) in the period 07/2021 – 03/2022. Bounds report on the scenarios obtained from the sensitivity analysis run on the efficacy of vaccines over time.

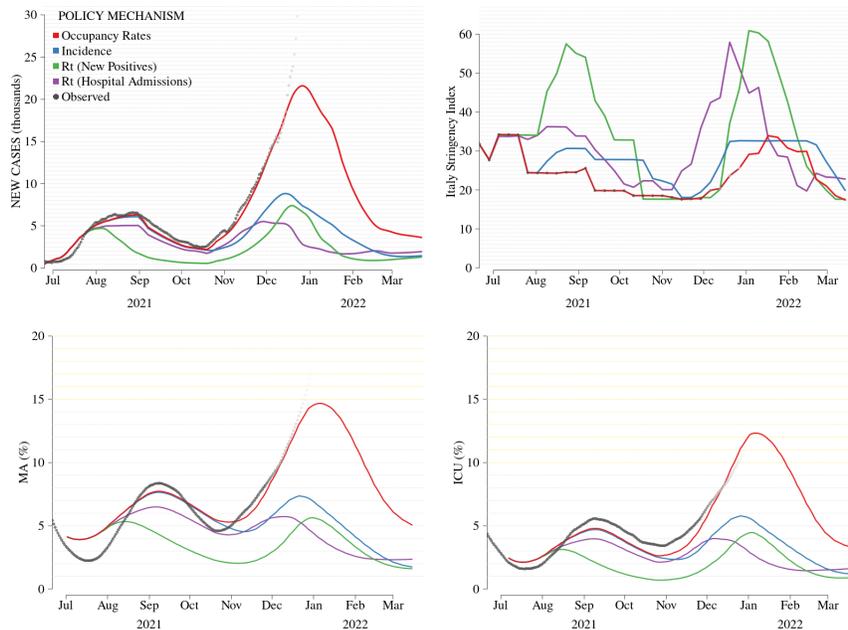


Figure 1: Comparison among mechanisms, *Actual rollout*. From left to right and top to bottom: new cases (thousands), Italy Stringency Index (ItSI) [20], occupancy rates in non critical medical areas (MA) and intensive care units (ICU). The mechanisms evaluated are: i) *Occupancy rates*, reproducing the mechanism operating in Italy from the end of July 2021, ii) *Incidence*, and iii) *Rt (New Positives)*, mimicking the policy frameworks operating, respectively, from May to July 2021 and from March to May 2021, and iv) *Rt (Hospital Admissions)*, fictitious, reproducing *Rt (New Positives)* while replacing the reproduction number, *Rt*, computed on new cases with the one on hospital admissions. The hypotheses underlying *Actual rollout* are described in the Methods and the Supplementary information.

First, *Occupancy rates* is the one that leads by far to the highest incidence (Fig. 1, top-left panel), which results in the highest occupancy rates in the hospitals (Fig. 1, bottom panels). Indeed, under this scheme, containment measures are less responsive to changes in epidemic conditions, which entails relatively longer waves of infections. At the same time, this low responsiveness implies a material reduction in the restrictiveness indicator as compared to the other policy frameworks (Fig. 1, top-right panel).

Second, *Rt-New positives* guarantees consistently relatively fewer infec-

tions and hospitalisations but at the cost of stricter containment measures. By relying on the effective reproduction number of detected cases, the mechanism determines a swift increase of restrictions (Fig. 1, top-right panel) during the summer wave (Fig. 1, top-left panel). However, the low incidence achieved at the beginning of the fall, combined with the progress in the vaccination campaign, allows for a delayed wave and a relatively low level of restrictions until November-December 2021. Restrictions increase steeply at the beginning of 2022, when the epidemic also accelerates under this mechanism. Over the entire simulation period, *Rt-New positives* reduces reported cases by about 4.800 as compared to *Occupancy rates* mechanism and, on average, hospital bed occupancy would be 4.2 p.p. lower in non critical medical areas (3.4 p.p. in ICU). At the same time, the Stringy Index is about 40% higher, which implies considerable increase in the socio-economic costs related to social distancing provisions.

Incidence and *Rt-Hospital admissions* occupy intermediate positions in the health-stringency spectrum. The two mechanisms are associated with similar cases and hospital admissions, and the overall level of restrictions is comparable until fall 2021, albeit with different timing. *Rt-Hospital admissions* tends to react more promptly to a change in epidemic conditions than *Incidence*. Noticeably, the progress in the vaccination campaign achieved by the end of the year determines that the hospital bed occupancy rates associated with *Rt-Hospital admissions* and *Incidence* are relatively close to each other. However, different from the summer wave, the former triggers substantially stricter restrictions than the latter.

The evaluation of the different mechanisms may also depend on external conditions regarding, for instance, the characteristics of the virus, the evolution of the vaccination campaign, vaccine efficacy, and waning protection, etc. In particular, vaccine administration has been a key policy variable available to tackle the Covid-19 epidemic since the presence of vaccines shapes the relation between restrictions and epidemic outcomes. [55, 58] For example, lower vaccine protection or coverage may make the adoption of highly responsive mechanisms desirable to limit the burden of a massive epidemic outbreak on the national health system. To test how different mechanisms respond to different external conditions, we conduct simulations assuming higher and lower levels of vaccine coverage, in which vaccine uptakes are exogenously given. We label these simulations *Optimistic rollout* and *Pessimistic rollout*, respectively. *Optimistic rollout* (Fig. 2) assumes a faster rollout, a larger final uptake among the population, and a faster deployment of the third dose

(booster). Conversely, *Pessimistic rollout* (Fig. 3) relies on a slower and less extensive rollout than observed. All scenarios account for uncertainty in the vaccination-induced immunity (see Section Methods and the Supplementary Material for further details).

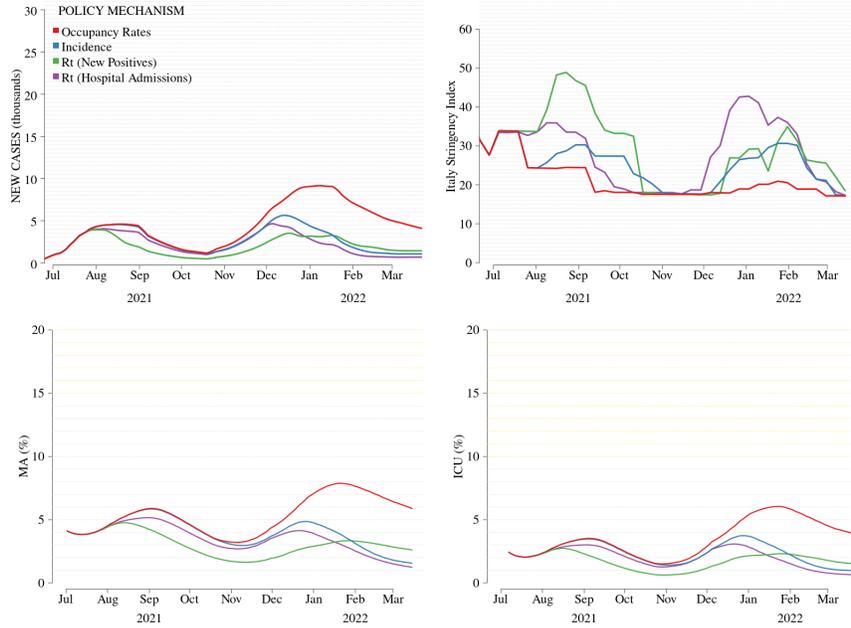


Figure 2: Comparison among mechanisms, *Optimistic rollout*. From left to right and top to bottom: new cases (thousands), Italy Stringency Index (ItSI) [20], occupancy rates in non critical medical areas (MA) and intensive care units (ICU). The mechanisms evaluated are: i) *Occupancy rates*, reproducing the mechanism operating in Italy from the end of July 2021, ii) *Incidence*, and iii) *Rt (New Positives)*, mimicking the policy frameworks operating, respectively, from May to July 2021 and from March to May 2021, and iv) *Rt (Hospital Admissions)*, fictitious, reproducing *Rt (New Positives)* while replacing the reproduction number, *Rt*, computed on new cases with the one on hospital admissions. The hypotheses underlying *Optimistic rollout* are described in the Methods and the Supplementary information.

Results confirm that vaccination coverage is a crucial variable interacting with the policy mechanisms. In the counterfactual *Optimistic (Pessimistic) rollout* scenario, new cases, occupancy rates of hospital beds, and the ItSI

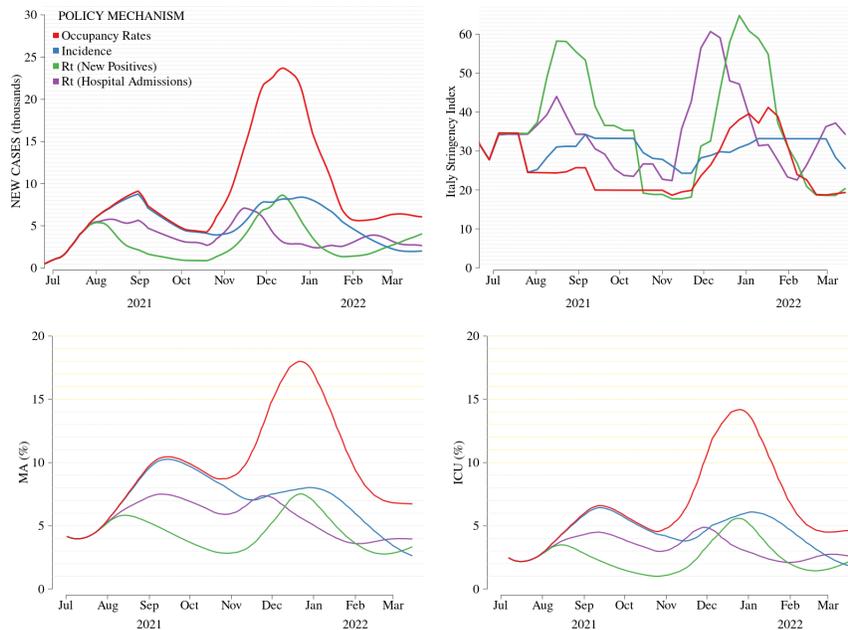


Figure 3: Comparison among mechanisms, *Pessimistic rollout*. From left to right and top to bottom: new cases (thousands), Italy Stringency Index (ItSI) [20], occupancy rates in non critical medical areas (MA) and intensive care units (ICU). The mechanisms evaluated are: i) *Occupancy rates*, reproducing the mechanism operating in Italy from the end of July 2021, ii) *Incidence*, and iii) *Rt (New Positives)*, mimicking the policy frameworks operating, respectively, from May to July 2021 and from March to May 2021, and iv) *Rt (Hospital Admissions)*, fictitious, reproducing *Rt (New Positives)* while replacing the effective number, *Rt*, computed on new cases with the one on hospital admissions. The hypotheses underlying *Pessimistic rollout* are described in the Methods and the Supplementary information.

would all reach remarkably lower (higher) levels than the baseline. As expected, vaccines effectively slow down the spread of the disease in the population, reduce the share of infected requiring medical treatment, and drag down the level of restrictions needed to contain the epidemic by acting effectively on the respective underlying indicator. For instance, under the *Optimistic rollout* scenario average MA occupancy rates are 0.5-1.9 p.p. lower than in the *Baseline*, with the difference varying across the mechanisms. Indeed, the *Optimistic rollout* is characterised by a lower level of heterogeneity in

terms of cases and hospital admissions across the mechanisms. *Rt-New positives* is still associated with the lowest number of daily newly reported cases (2,074 on average throughout the considered period), but the gain in terms of lower hospitalisations is considerably reduced with respect to the baseline exercise. Conversely, in this favourable scenario, health outcomes under *Occupancy Rates* are closer to those produced by the other mechanisms, while it still allows for a material reduction of the restrictions (see Figure 2, top-right panel). The difference in MA occupancy rates between *Occupancy Rates* and *Rt-New positives* is about 2.2 p.p. on average (1.8 for ICU), while the Stringency Index remain about 40% higher under the *Rt-New positives* mechanism. This evidence suggests that a policymaker aiming to reduce restrictions may prefer a milder policy framework, such as *Occupancy Rates*, when external conditions are particularly favourable (e.g., high vaccination coverage or low transmissibility of the virus).

Results are much more heterogeneous under *Pessimistic rollout*. In this case, *Occupancy Rates* mechanism leads to a substantial increase of hospitalisations and more impactful and persistent waves than the other mechanisms. Restrictions are still lower during the summer when favourable climatic conditions allow for lower transmissibility but tend to increase substantially in the fall-winter wave. *Occupancy rates* determines a level of ItSI that is even larger than those implied by *Incidence* during the same wave. Then, restrictions under *Occupancy rates* are not even far from that reached with other mechanisms (-15.3% compared with *Incidence*, -28.6% compared with *Rt-New Positives*), but the delayed response leads to levels of bed occupancy of ICUs and medical areas that are about twice as high as those obtained with the other mechanisms. More responsive schemes, like those that rely on reproduction numbers, in this unfavourable scenario, materially reduce hospital admissions. On average, restrictions associated with these mechanisms are quite high, but the differences from the other mechanisms are smaller than those found in more favourable scenarios. In this contest, *Rt-Hospital admissions* seems a valuable alternative to *Rt-New positives* in place in Italy throughout the spring of 2021. While the two mechanisms's restrictions are close during the winter wave, *Rt-Hospital admissions* is much more lenient than *Rt-New positives* during the previous summer wave.

Fig. 4 summarises the trade-off between epidemic/health outcomes and restrictions under different scenarios and policy mechanisms.

The integration of endogenous mitigation responses in epidemic models may prove useful in various applications, beyond the comparison between

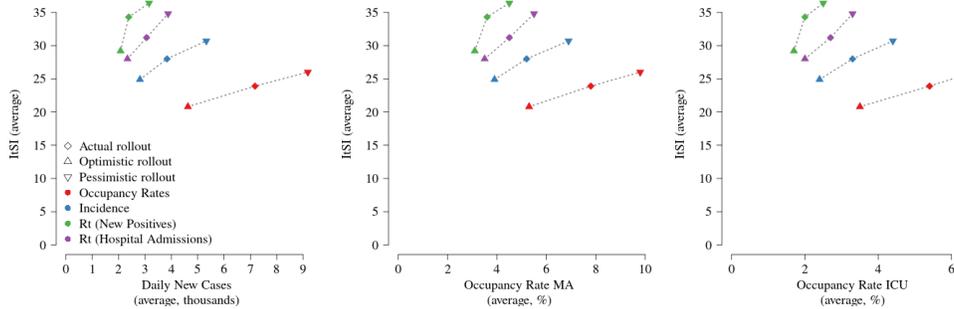


Figure 4: Trade-off between average restriction levels, as measured by the ItSI, and the average values of daily reported new positives (left panel), MA occupancy rate (middle panel), ICU occupancy rate (right panel) under each considered scenario (*Actual*, *Optimistic*, and *Pessimistic rollout*) and mechanism (*Rt-New positives*, *Incidence*, *Occupancy rates*, *Rt-Hospital admissions*) in the period 07/2021 – 03/2022.

different policy mechanisms. As we show validating the model in the Supplementary Information, taking into account self-adaptive NPIs allows simulation results to track the historical epidemic data much more precisely than those of models with restrictions fixed over time. This feature can be exploited also in projection exercises, aiming at investigating the possible future trajectories of epidemic variables and restrictions. Indeed, simulations based on the model presented in this work has been used to incorporate the projections of epidemic variables in forecasting models targeting the growth of Italian Gross Domestic Product. [6]

Taking into account the reaction of containment policies is crucial also to construct counterfactual analyses and provide ex post evaluations of the effects of a given exogenous event. For example, in the analyses described above we have investigated the effects of different vaccine rollout taking into account the possible changes in restrictions. In the Supplementary Information we provide an additional example of possible counterfactual analyses that can be conducted with the proposed modelling framework. In particular, we assess the determinants of the divergence in the epidemic between the United States and the European Union observed in the first half of 2021. Since late February 2021, the United States had been showing a lower incidence than most EU countries, despite a larger increase in community mobility. The faster vaccination rollout in the United States in the first phases

of the vaccine campaign may be seen as a possible explanation of this divergence. However, another important factor could have been the prevalence of a particular variant: at the time, a more contagious strain of the virus (the Alpha variant) was more widespread in the European Union than in the US. The proposed modelling framework can be helpful to disentangle the contribution of each component. We conduct a counterfactual analysis for the period February-May 2021 in which we apply to Italy the more favourable conditions prevailing in the United States in terms of vaccination rollout and variant prevalence. A delayed diffusion of the new variants would have reduced the number of new cases by 71.1% and the severity of restrictions in place. A faster vaccine rollout would have allowed a further relaxation of the policies and an additional drop in cases by 30.7%. Results suggest that being able to postpone the diffusion of these variants through controls on international movements and by identifying, isolating, and monitoring new outbreaks can help curb the epidemic, with benefits of the same order as those associated with a substantial acceleration in the vaccine rollout.

3 Discussion

At the end of 2020, to counter the spread of Covid-19, many countries resorted to geographically differentiated measures, contingent upon epidemic indicators. While this approach offers several advantages compared with discretionary strict nationwide interventions, it also requires assessing the adequacy of a policy in a framework in which the policymaker commits to a course of actions and external factors rapidly evolve (e.g., diffusion of new variants of concern, the progress of the vaccine campaign). Dynamic assessment of policy effectiveness is crucial to projecting credible epidemic scenarios and related restrictions over different time horizons. The framework presented in this paper can help policymakers choose the appropriate criteria to mitigate the epidemic (health costs) while minimising the severity of restrictions (socio-economic costs).

A key aspect, seemingly overlooked by standard epidemiological models, is the interplay between containment policies and the evolution of the pandemic. In this paper, we account for this interaction by embedding rule-based self-adaptive policy restrictions into an epidemic model, and we show the insights that such an enriched model can provide. We find that different rules translate into diverse outcomes regarding restrictions and the epidemic.

The complex interaction between restrictions and uncertain epidemiological conditions can even magnify the differences across viable regulatory frameworks.

The extension of the SIR model to include different self-adaptive policy mechanisms presented in this paper replicates the Italian framework operating since November 2020, which has assigned regions to restrictions' tiers depending on specific epidemic indicators. In this way, we can simulate the evolution of the variables of interest during the diffusion of the Delta variant over the period July 2021-March 2022. As NPIs are not the only tool available to the policymakers, we also consider alternative scenarios on the vaccination rollout to provide a spectrum of outcomes that policymakers may face and test how the policy mechanisms operate in different conditions. Introducing a self-adaptive rule-based policy mechanism is substantially different from exploring the set of available policies with a standard SIR model because, in the former case, NPIs are automatically activated and deactivated depending on their effects of the epidemic's trajectory.

Simulations show that policy mechanisms based on reproduction number reduce the impact on the health system compared to alternative mechanisms based on stock variables (e.g., hospital bed occupancy rates or incidence), especially with low vaccine coverage among the population. The rationale is that it takes time before the spreading of the disease raises the occupancy rate or the incidence to the threshold that triggers restrictions. Likewise, the effects of NPIs require time to show up in the data since some degree of inertia may characterise the immediate evolution of the epidemic. Conversely, more responsive mechanisms generally entail stricter containment measures. The trade-off between health outcomes and the level of social interactions ensured by the different regimes crucially depends on the external context. In favourable conditions, as in the considered scenario with very high vaccination coverage, milder policy schemes guarantee a sizable reduction in restrictions with a relatively small increase in cases and hospital admissions. On the other hand, with lower levels of vaccination, more responsive mechanisms provide a substantial reduction of cases and hospitalisations, thanks to NPIs which are activated earlier and are more restrictive. Clearly, further elements, which are not modelled here, may affect this trade-off (e.g., the availability of effective treatments, the costs associated with long-term sequelae of Covid-19 infections, loss in school days or working hours linked to quarantines). Ultimately, the evaluation of the trade-off depends on the policymaker's (and public opinion's) preferences over epidemiological, economic,

and social outcomes. By pinning down some key variables, our framework helps making such assessment more transparent, while being flexible enough to include other aspects characterising the trade-off.

While we consider many possible sources of uncertainty in our simulations, we remain agnostic on some other relevant factors. For example, the lack of robust evidence on contact tracing and the role of school transmission makes it harder to predict the effectiveness of policies, which also depends on the ability of the system to identify and isolate infected individuals promptly. We tackle these issues by including community mobility indicators and calibrated elasticities to describe the impact of tier-related provisions on the epidemic. Furthermore, notification rates are likely to vary over time following an inverse relation with the incidence of infections among the population. Also vaccination rates, which we treat as exogenous for the sake of simplicity, are likely to be influenced by the policy framework and the evolution of epidemic and health conditions. [64, 62] Individual-level information on testing by region and age group would be necessary to obtain reliable estimates of time-varying detection rates. For this reason, quantitative outcomes associated with different epidemiological scenarios are just illustrative and serve to evaluate the potential interplay between the disease spread and endogenous mechanisms to counter an increase of Covid-19 infections. Epidemic evolutions are subject to many sources of uncertainty beyond those surrounding the model parameters, such as the emergence of other insidious variants (e.g., the Omicron variant, spreading across European Countries since late November 2021), waning immunity, radical changes in the policy framework, variations in people’s compliance with the rules. As a further layer of complexity, these sources of uncertainty also interact with each other. For example, individual behaviour may change over time or across locations due to the so-called “lockdown fatigue” or the adaptation to the varying external conditions - e.g., vaccination status, low/high number of infections. Moreover, since an epidemic is a highly non-linear phenomenon, the evaluation of the costs associated with the restrictions may substantially vary depending on the state of the epidemic itself. Finally, although our framework is general enough to be adapted to a large number of rule-based mechanisms, as the proposed fictitious examples show, we do not model the choice of the optimal mechanism because this problem would require, among others, to embed policymakers’ preferences into the set of possible outcomes. In the background of our analysis, there is an important warning. Informing rule-based policies requires the production of timely and reliable data. Poor information may

lead to inadequate measures and jeopardise public trust, which is crucial to contain a pandemic successfully.

Despite these difficulties, including a policy-response algorithmic component in a fully-fledged epidemic model constitutes an essential step forward in designing evidence-informed policy responses, especially within a rule-based framework. Throughout the Covid-19 pandemic, many valuable contributions have tried to bridge the gap between epidemiology and economics. [4, 56, 2, 26] To embed containment policies into an epidemiological model is key to designing policies that improve socio-economic and sanitary outcomes. Our enriched model provides a comprehensive and realistic framework to evaluate the potential impact of the pandemic and related restrictions, which is also essential for economic forecasting since we show that the inclusion of self-adaptive policies is essential to track the historical evolution of epidemic outcomes and restrictions. The proposed framework can be easily employed to evaluate rule-based policies *ex ante* and *ex post* in other countries with an appropriate fine-tuning of the parameters. The availability of a modelling tool such as the one presented in the paper supports informed choice among alternative policy response mechanisms.

4 Methods

The core of our framework is the interaction between the SARS-CoV-2 transmission and restrictions. We model the transmission for each Italian region and autonomous province with an age-structured compartmental model, which extends the workhorse SIR framework [47] by accounting for different courses of the symptomatic disease, variants of the virus, effects of temperature, types of vaccines, and progress in the vaccination campaign (Fig. 5). Regarding vaccines, we incorporate the current available evidence regarding their waning immunity against infection and protection against severe disease [29, 49, 74] Every week, regional state variables contribute to deriving epidemiological indicators (e.g., case incidence, reproduction number, hospital occupancy rates). Then, the indicators are fed to an algorithmic component, which provides tiers of restrictions for the subsequent week, mimicking the response mechanisms adopted by the Italian MoH since November 2020. Tiers define the containment policies for the ensuing week, which affect the consequential evolution of the epidemic. In turn, the implied evolution of the epidemic determines the path of future measures, and so on. We stratify

the Italian population by geography and age. Concerning the former, we follow the Nomenclature of Territorial Units for Statistics – Level 3 (NUTS 3), dividing the Italian territory into 19 regions and 2 autonomous provinces, yielding a metapopulation approach. In line with this, we introduce region-specific fixed effects to reflect the heterogeneity across distinct geographical units. Regarding the age classification, we consider five distinct groups: 0-12, 13-18, 19-64, 65-79, 80+. Besides the described stratification, we augment the model with additional compartments, accounting for different courses of the symptomatic disease, vaccine types, and virus variants. Finally, we allow for a time-varying parametrisation reflecting changes in the seasonal conditions, coverage, and efficacy of the vaccines by region and targeting group.

The evidence available through the Italian National Institute of Health (Istituto Superiore di Sanità, henceforth ISS) shows that two variants were highly prevalent in the country in the second half of 2021: Alpha, until June, and Delta, from July onwards. [41, 40] Features of the variants were parametrised according to the available literature, allowing Delta to be significantly more transmissible than Alpha [65] and twice as likely to result in hospitalisation among non-vaccinated individuals [53]. In December, a new variant, Omicron, spread in the country. Although the simulations cover the period July 2021-March 2022, we abstract from the emergence of the Omicron variant to better appreciate the functioning of the different policy mechanisms under different conditions. Limiting the simulation sample to the actual period of prevalence of the Delta variant (i.e., July-December 2021) would have entailed a less accurate comparison of health and restrictiveness outcomes, as the timing of restrictions and epidemic waves vary across mechanisms. Considering a longer time sample reduces this potential bias as the simulation period is long enough to observe the descending part of the epidemic curves under all the scenarios and policy mechanisms. Conversely, including the insurgence of the Omicron variant in the simulations would have added an additional source of uncertainty in model’s parametrisation and complicated the interpretation of the results. Nonetheless, we tests that results are qualitatively unchanged when including the Omicron variant in the model

The vaccination campaign in Italy has relied on four approved vaccines: two mRNA vaccines (Comirnaty by Pfizer/BioNTech and Spikevax by Moderna) and two viral vector vaccines (Vaxzevria by Oxford University and AstraZeneca and the Covid-19 Vaccine by Janssen/Johnson&Johnson). Given

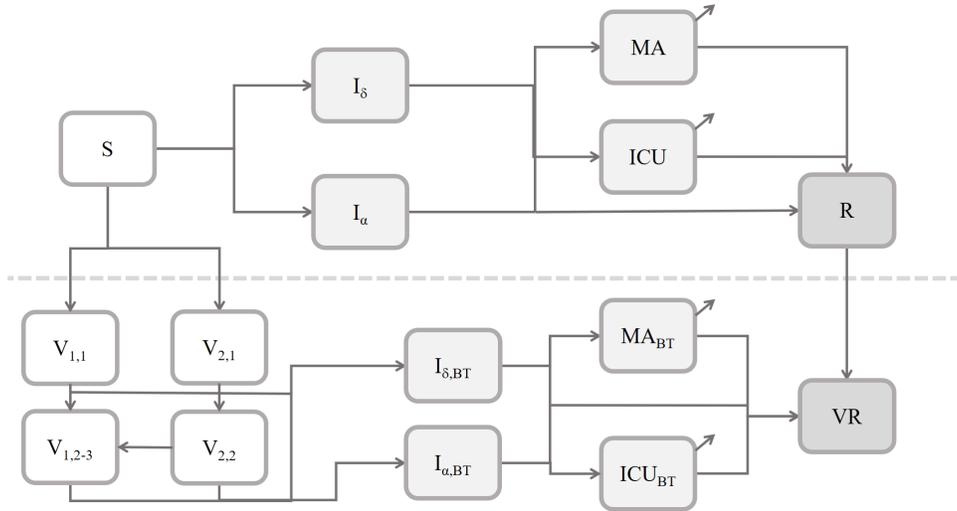


Figure 5: Simplified representation of the epidemiological compartmental model. Model compartments: Susceptible to the virus (S), infectious with Delta type virus (I_δ) and with Alpha (I_α) variant, hospitalised in the medical area (MA) and intensive care unit (ICU), recovered from natural infection (R), immunised with the first group of vaccines (first and second/third dose, respectively, $V_{1,1}$ and $V_{1,2-3}$) and with the second group of vaccines (first and second dose, respectively, $V_{2,1}$, $V_{2,2}$), breakthrough infectious with Delta ($I_{\delta,BT}$) and Alpha variant ($I_{\alpha,BT}$), hospitalised with breakthrough disease (MA_{BT} , ICU_{BT}) and recovered from breakthrough infection (VR). The dashed line separates the dynamics associated to natural infections from those relating to vaccinated individuals. See the Supplementary information for details.

the similar profiles, we group the four vaccines into two classes: 1) Comirnaty/Spikevax, 2) Vaxzevria/COVID-19 Vaccine Janssen. The two classes differ in the administration mode, efficacy in preventing infections, hospitalisations, and deaths. We differentiate the protection against the disease among immunised individuals by the number of doses received - first, second or third - and by variant, as vaccines appear less effective against the Delta than Alpha [72]. However, they are still highly protective among fully vaccinated individuals [76] and prevent hospital admissions in more than 90% of cases [53]. The available evidence also shows that the protection associated

with vaccination wanes over time. We account for this finding by modelling age-dependent vaccine-specific reduction in protection against infection and risk of hospitalisation over time. Alongside effectiveness, we track differences in vaccination uptakes across regions and age groups by using historical data until November 2021 available through the Github repository maintained by the Italian Civil Protection [42].

We consider three scenarios for vaccination campaign. The first one is *Actual rollout*, which is based on historical data. Next, *Optimistic rollout* assumes a faster rollout than observed between June and November (20% faster in the second and third age groups, 55% for the fourth age group, and 105% faster for the fifth age group). Finally, *Pessimistic rollout* assumes a slower rollout than observed (80% of actual doses for all age groups between June and December). For the period December 2021-March 2022, we consider a reprise of first doses in all scenarios, which should fit the increase due to the extension of the Covid-19 certificate. However, the slowdown of new first doses differs across scenarios, with *Pessimistic* (*Optimistic*) *rollout* showing a faster (slower) reduction of first doses than *Actual rollout*. Regarding boosters, we replicate the policy enacted by the Italian government in *Actual rollout*. In September, boosters administration was open to the elderly 6 months after the second dose. [43] Later on, the Italian government extended the criteria for eligibility to younger cohorts and shortened the minimum distance between the second and third doses first to 5 months [44] and then to 4 [45]. *Optimistic* (*Pessimistic*) *rollout* assumes a fast (slow) deployment of boosters to the eligible individuals. Moreover, vaccinated individuals may access boosters after 4 months after full vaccination in *Optimistic rollout*. The allocation of boosters works according to a first-in-first-out principle. In other words, since we do not have individual-level information on the time span between the vaccinations, we assume that individuals with the older vaccination are the first to receive a booster.

Regional effects are calibrated according to mobility data available in the Google Covid-19 Community Mobility Reports. [52] Seasonal effects hinge on historical weather reports and are such that an increase of one degree Celsius decreases the reproduction number by 0.005 based on available evidence in the literature. [13]

A key component of our framework is the algorithmic mechanism underlying NPIs. In our setup, a fixed set of criteria define regional tiers based on the epidemiological indicators produced by the model. The Italian government has enforced restrictions relying on a set of epidemic indicators since

November 2020. The indicators have been used by the Italian MoH to assign each region to a tier for restrictions every week (yellow, orange, or red zone, initially, with growing associated level of risk; later on, the government also introduced a white low-risk zone). While the government updated the criteria for the ruling mechanism over time, the prescriptions of NPIs associated with each tier have been mostly consistent. Because of that, the restriction level directly acts upon the number and intensity of social contacts for a given tier, increasing or reducing them in the white and red zone, respectively.

We exploit the initial implementation period of the tier system (November-December 2020) to calibrate the parameters and first assess the model’s performance. This sample is an appropriate training set since new variants and vaccines had yet to influence the course of the epidemic materially, and the policy mechanism had been constant during the period. In this setting, we pin down the basic model parameters limiting the possible influence of confounding factors.

We initialise the model to match actual epidemic data on 9 November 2020, which is the starting point of the first simulation. We first pass regional restrictions (also policies) to the model based on historical data to derive regional-specific effects and the tier-specific mobility elasticity of the force of infection.

Then, we validate our model using the third wave caused by the Alpha variant. For the initialisation, we match actual epidemic data on 18 January 2021: we estimate about 13.6% of the population was already immune to the virus at that date, due to past infection. Furthermore, we calibrate the initial prevalence of the Alpha variant in each region by using a grid search method in which the value range for each region was set according to data by the ISS on sequenced SARS-CoV-2 genomes. In particular, the first available data on the regional prevalence of new variants rely on a sample of cases detected on 16 February 2021. [38] Additional surveys were conducted on 18 March 2021 [37] and 20 April 2021 [39]. The pattern of prevalence of the new variant generated by the model is broadly in line with survey results (see Supplementary information for details).

Supplementary Information

A.1. The Compartmental Metapopulation Model

We assume the population to be fully susceptible to Covid-19 at the beginning of the pandemic. We successively estimate the regional share of the population that never contracted the virus up to the start of our simulation period by exploiting detailed information on cases, fatalities, and hospitalisations provided by the Italian National Institute of Health (Istituto Superiore di Sanità, ISS) in combination with estimates on age-specific Infection Fatality Rates (IFRs) drawn from the literature. Before introducing the model, we define some basic notation. Let $r = 1, \dots, 21$ denote an Italian region (we treat the autonomous provinces of Bolzano and Trento as regions). We use interchangeably “region” and “geographical entity”. We consider five age groups a , with $a \in \{0 - 12, 13 - 18, 19 - 64, 65 - 79, 80+\}$. Time is discrete, with t denoting the day. Finally, let p represent a policy, with $p \in \{\text{white, yellow, orange, red, semi-lockdown}\}$. We note that orange may also represent the yellow zone with additional restrictions, red may also represent orange with additional restrictions, and semi-lockdown represents the red zone with additional restrictions as it was regulated during March-April 2021. For each region r and age group a , the number of individuals that have already contracted the virus up to day t , $INF_{a,r}(t)$, is estimated as:

$$INF_{a,r}(t) = \sum_{s=0}^t \frac{\mu_{a,r}}{IFR_a} H_{a,r}(s)$$

where $H_{a,r}(s)$ is the number of new hospitalisations in region r at time s ; $\mu_{a,r}$ is the ratio between hospitalisations and fatalities from the ISS Covid-19 surveillance data[68] for region r and age-group a ; IFR_a is the age-specific Infection Fatality Rate.[61] We compute the notification rate for each region r and age group a , $\delta_{a,r}(t)$, by taking the ratio between the cumulative sum of notified cases up to day t for region r and age group a , $CASES_{a,r}(t)$, and estimated infections, $INF_{a,r}(t)$:

$$\delta_{a,r}(t) = \frac{CASES_{a,r}(t)}{INF_{a,r}(t)}$$

To account for changes in testing strategies, we calibrate the values for the notification rate based on the period ranging from 1 October 2020 to 18

January 2021. Age- and region-specific rates are used to initialise the model and simulate the number of detected cases from actual new infections, with average estimated notification rates are 36.0%-49.1%.

The model accounts for the two main trajectories: the dynamics of natural infections and that induced by vaccination. Dynamics are described by the following system of differential equations:

$$\begin{aligned}
S'_{a,r}(t) &= - \left(\sum_j \lambda_{j,r,a,p}(t) + \sum_k \eta_{k,a}(t) \right) S_{a,r}(t) \\
I'_{j,a,r}(t) &= \lambda_{j,r,a,p}(t) S_{a,r}(t) - \gamma I_{j,a,r}(t) \\
nICU'_{a,r}(t) &= \gamma(1 - \iota_a) \sum_j \xi_{j,a} I_{j,a,r}(t) - \gamma_{nICU} nICU_{a,r}(t) \\
ICU'_{a,r}(t) &= \gamma \iota_a \sum_j \xi_{j,a} I_{j,a,r}(t) - \gamma_{ICU} ICU_{a,r}(t) \\
R'_{a,r}(t) &= \gamma \sum_j (1 - \xi_{j,a}) I_{j,a,r}(t) + (1 - \alpha_a)(\gamma_{nICU} nICU_{a,r}(t) + \gamma_{ICU} ICU_{a,r}(t)) - \sum_k \eta_{k,a}(t) R_{a,r}(t) \\
V'_{k,a,r,1}(t) &= \eta_{k,a}(t) S_{a,r}(t) - (\sigma_k + \sum_j (1 - \varepsilon_{k,j,1}) \lambda_{j,r,a,p}(t)) V_{k,a,r,1}(t) \\
V'_{k,a,r,2}(t) &= \sigma_k V_{k,a,r,1}(t) - \sum_j (1 - \varepsilon_{k,j,2}) \lambda_{j,r,a,p}(t) V_{k,a,r,2}(t) \\
BTI'_{j,a,r}(t) &= \lambda_{j,r,a,p}(t) \sum_{k,d} (1 - \varepsilon_{k,j,d}) V_{k,a,r,d}(t) - \gamma BTI_{j,a,r}(t) \\
nICU'_{a,r,BT}(t) &= \gamma(1 - \iota_a) \sum_j \xi'_{j,a} BTI_{j,a,r}(t) - \gamma_{nICU} nICU_{a,r,BT}(t) \\
ICU'_{a,r,BT}(t) &= \gamma \iota_a \sum_j \xi'_{j,a} BTI_{j,a,r}(t) - \gamma_{ICU} ICU_{a,r,BT}(t) \\
VR'_{a,r}(t) &= \sum_k \eta_{k,a}(t) R_{a,r}(t) + \gamma \sum_j (1 - \xi'_{j,a}) BTI_{j,a,r}(t) + (1 - \alpha_a)(\gamma_{nICU} nICU_{a,r,BT}(t) + \gamma_{ICU} ICU_{a,r,BT}(t))
\end{aligned}$$

where $j = 1, 2$ refers to variant types, $k = 1, 2$ denotes vaccine groups, and $d = 1, 2$ denotes first and second doses, respectively.

Model compartments are:

- **S**: *Susceptible individuals* are at risk of being infected by the virus. The per capita rate $\lambda_{j,r,a,p}(t)$ at which individuals acquire the infection is called Force of Infection (FoI), defined for the wild and variant types. The FoI takes different values according to time, variant type, age class, region, and ongoing policy and, it follows from the equation

$$\lambda_{j,a,r,p}(t) = \beta^j \beta^{a,j} (1 - \phi^p) \beta^r \sum_{a'} \beta^{p,a,a'} C_{a,a'} \frac{Inf_j^{a',r}(t)}{P^{a',r}(t)}.$$

The proportion of infectious individuals (last term of the right-hand side) stems from the model at each time step. In detail, $Inf_j^{a,r}(t)$ represents the number of infectious individuals:

$$Inf_j^{r,a}(t) = I_j^{r,a}(t) + \tau I_{j,BT}^{r,a}(t),$$

where $0 \leq \tau \leq 1$ quantifies the reduced transmissibility of breakthrough infections, i.e., due to vaccine failure. Throughout our analysis, we assume $\tau = 0.55$ as sensitivity analysis on this parameter shows that the overall transmission is not significantly affected by its value. $P^{a,r}(t)$ corresponds to the overall number of individuals at time t by age a and region r and is obtained as the sum of all compartments. The derived infectious proportion of the population is combined with terms:

- β_j represents variant-specific contributions to the FoI, with $j = 1, 2$. Both values are estimated based on an alternate grid search procedure, as described below, and optimal values are $\beta^1 = 0.015$ and $\beta^2 = 0.022$ to account for the increased transmissibility of the Alpha and Delta variants. For the Delta variant, the specific contribution is assumed to increase by 1.64(1.4, 1.9) times, compared to β^2 [53].
- $\beta^{a,j}$ terms represent age-class specific susceptibility to virus type j . For the wild type, we consider the following values: 0.58 among children and teenagers, 1.0 for adults, and 1.65 for people aged 65 or older.[35] Values for the variant type Alpha are estimated by a grid search to account for the increased transmissibility among younger people. Estimated values are 1.0 among children, 0.68 for teenagers, and 0.86 for adults. Due to the lack of evidence, we use the same parametrisation for the Delta variant. As a remark, other than the purely medical information, we expect such values to capture also the different behaviour characterising age classes.
- ϕ^p represents mitigation effects on transmission dynamics, as induced by the sets of restrictions adopted within each policy regime of the tier system. Values derive from the retail and recreation mobility indicator in the Google Community Mobility Reports.[52] The indicator exhibits the highest correlation with the values of the reproduction number at the regional level. Mobility reductions range from 4.2% (white zone), to 40% (semi-lockdown regime).

We account for policy changes during summer 2021 by considering data in May-June 2021 and mobility levels during summer 2020 when similar rules were in place.

- β^r terms summarise the region-specific effects and responsiveness to the mitigation strategies adopted. Values were obtained by grid-search, minimising the mean square error between the observed and estimated regional incidences throughout the second wave (November and December 2020). Baseline estimates were separately derived for each region through an optimisation routine and vary from 0.90 (Basilicata) to 1.25 (Lombardia), with the population-weighted average equal to 1.09. For simulations of longer-time horizons, we also take into account the possible contribution of seasonal conditions in reducing virus transmission by introducing a regional-specific correction factor that depends on the deviations of temperatures from the median value over the year. Literature finds an inverse relation between temperatures and SARS-CoV-2 transmission, which may be not only strictly related to the direct effects of higher temperatures on the virus but also to other causes, as the fact that social interactions may occur more frequently outdoors with warm weather conditions.[54] Nonetheless, there is no clear consensus on the quantitative effects of temperatures.[13] Based on the available evidence, we assume that an increase of one degree Celsius decreases the regional effects by 0.015. Given the high uncertainty about this effect, we also consider the range of [0.005-0.025]. Estimated regional effects are depicted in Figure 6, together with their ranges of variation due to the temperature effects. We obtain daily average temperatures for all Italian regions over the past ten years (downloaded from www.ilmeteo.it) Given the high transmissibility of the Delta variant and the unprecedented outbreaks also observed in the warmest areas of the globe, we assume a low-temperature effect on transmissibility (0.005). We also explore the effect of considering alternative values for this parameter in the range of [0.0025 – 0.0075].
- $\beta^{p,a,a'}$ and $C_{a,a'}$ represent the average number of effective daily contacts between individuals from age classes a and a' , as designed by the Polymod matrix[60]. We exploit $\beta^{p,a,a'}$ to reduce the number

of contacts among children and teenagers only, according to the policies adopted on school closures and remote learning, i.e., $\beta^{p,a,a'}$ differs from 1 if $a = a'$ and $a \in \{0 - 12, 13 - 19\}$. We calibrate the values for the two age groups using data on mobility and school restrictions and validate them throughout the available periods. We set them to 0.3 for the red zone, 0.5 for the orange one, 0.7 for the yellow one, and 0.75 for the white one. Over the summer, we set 0.6 as the baseline and consider the range of 0.5-0.8 for the sensitivity analysis.

Beyond natural infection, susceptible people may leave the compartment following vaccination, according to monthly age-specific coverage rates $\eta_{k,a}(t)$, for vaccine group k .

- **V_{1,1}, V_{2,1}**: We consider two sets of vaccines, equally effective against the wild and variant types. The first set ($k = 1$) consists of Pfizer BioNTech and Moderna vaccines, whereas the second includes the Oxford-AstraZeneca and Johnson & Johnson vaccines. The two vaccine types are administered based on different timing and are targeted to different age groups in line with the Government’s plan. The two vaccine groups also differ in their efficacy (see Table 2). We assume uniform coverage rates among geographical entities and do not account for regional specificities, e.g., delays, disruptions. Except for the Johnson & Johnson vaccine, all vaccines require two doses to reach full effectiveness. Since the marginal contribution of the single-dose vaccine is negligible (about 3.1% of the fully vaccinated people as of 31 January 2022), we assume that all vaccines belonging to group 2 require two doses for the sake of simplicity. We model such a setup by accounting for a first compartment, $V_{k,1}$, where susceptible vaccinees are transferred with age-specific coverage rate $\eta_{k,a}$, $k = 1, 2$. Once in the compartment, people may either acquire the disease due to vaccine failure – i.e., the complement to one of vaccine efficacy $\varepsilon_{k,1,d}$ – or receive the second dose with rates $\sigma_1 = 21\text{days}^{-1}$ and $\sigma_2 = 90\text{days}^{-1}$ and move to the respective compartment $V_{k,2}$.
- **V_{1,2}, V_{2,2}**: People who received both doses of vaccine group k are exposed to breakthrough infection, net of vaccine efficacy values $\varepsilon_{k,2,d}$. Details on vaccine efficacy by dose and variant are reported in Table 2.

- **I₁, I₂**: At each time step, susceptible individuals are exposed to the risk of acquiring the infection and becoming infectious with either the wild type or the variant. Throughout their stay in the infectious compartments, individuals contribute to the respective FoI. They finally move to the Recovered compartment, following a generation time γ^{-1} of 5.6 days[50] or are hospitalised in ICU or non-critical areas. In the former case, we assume that individuals no longer contribute to the FoI because they either recover from the disease or get tested and isolate themselves until complete recovery. As a technical remark, hospital admissions occur with a systematic delay of around 4 days in the latter case. Another technical assumption is that people in the infectious stages are not subject to any death risk by the disease.
- **I_{1,BT}, I_{2,BT}**: Vaccinated individuals that acquire the disease due to vaccine failure against virus type $j = 1, 2$ enter the corresponding infectious compartment, then leave it at a rate of γ . For the wild and Alpha type variants, the first dose of Pfizer BioNTech and Moderna vaccines confer $\varepsilon_{1,j,1} = 0.38\%$ (29%, 45%) protection against severe SARS-Cov-2 infection, whereas the Oxford-AstraZeneca and Johnson & Johnson were attributed $\varepsilon_{2,j,1} = 37\%$ (32%, 42%) efficacy against infections.[53] Efficacy values for second doses are $\varepsilon_{1,j,2} = 92\%$ (90%, 93%) and $\varepsilon_{2,j,2} = 73\%$ (66%, 78%). As already discussed, vaccinated individuals acquiring the breakthrough infection would eventually suffer an asymptomatic to mild infection, with zero risks of hospitalisation and death, and thus would exclusively contribute to the overall incidence of Covid-19 cases. This assumption implies that breakthrough infections result in neither hospitalisation nor death throughout the third wave. However, in the projection frameworks, a severe disease followed by hospitalisation and death is possible also for the vaccinated, though with a lower probability (see Table 2).
- **nICU, ICU, nICU_{BT}, and ICU_{BT}**: People leaving infectious compartments are either admitted to non-critical (non-ICU) or, when their conditions worsen, to intensive care units (ICU) or fully recover. To model *hospital admissions*, we retain a share $\xi_{j,a}$ of the individuals leaving **I_j** at a rate of γ , with $j = 1, 2$. $\xi_{j,a}$ represents the variant- and age-specific probability of hospitalisation among infected individuals. In the scenarios accounting for severe breakthrough infections, hospital

admissions into **nICUBT** and **ICUBT** occur according to $\xi'_{j,a}$, which is equal to $\xi_{j,a}$ scaled down by an average factor of 0.3 (0.15 – 0.45).[53] An age-specific proportion, ι_a , of hospitalised people is admitted to intensive care units, whereas the remainder is conveyed towards non-ICUs. Values for $\xi_{j,a}$ and ι_a are calibrated using individual information in the ISS database and increase with age. Hospitalised individuals leave the non-ICU and ICU stages at rates of γ_{nICU} and γ_{ICU} , respectively. Among these, an age-specific proportion dies according to an age-varying parameter α_a that is computed based on the ISS Covid-19 surveillance data on fatalities and hospitalisations.

- **R**: Recovered individuals from the natural disease move into the recovered compartment, where they are no longer susceptible to the virus throughout their stay. In line with the literature, we assume that immunity from natural disease cannot wane.[24]. The individuals of the **R** compartment with one of the two sets of vaccines available move into the stage of vaccinated individuals that are no longer susceptible to any SARS-CoV-2 infection, denoted as **VR**. This assumption seems to be reasonable in the context of infections related to Alpha and Delta, in which the overall number of reinfections was negligible. The initial share of recovered individuals in each geographical entity is estimated from hospitalisations and fatality rates as described above:

$$R_{a,r}(t_0) = INF_{a,r}(t_0) - \sum_s^{t_0} deaths_{a,r}(s)$$

- **VR**: Vaccinated individuals developing breakthrough disease from infection are assumed to leave the **BTI** compartment on average after five days and acquire complete immunity. Unlike the compartment **R** of individuals recovered from natural infection, subjects in **VR** are by definition no longer eligible for a vaccine.

| PARAMETER | VALUE [min, max] | NOTE |
|---------------------------------------|---------------------|------|
| γ^{-1} (generation time, days) | 5.6 | [50] |

| | | |
|--|--|--|
| $\xi_{w,a}$ (age-specific proportion of hospital admissions among infected individuals for wild type) | 0-12: 0.004 13-18: 0.004 19-64: 0.019 65-79: 0.062 80+: 0.119 | Own estimates from the ISS Covid-19 Surveillance data [68] |
| $\xi_{2,a}$ (age-specific proportion of hospital admissions among infected individuals for variant type) | 0-12: 0.006 13-18: 0.007 19-64: 0.031 65-79: 0.102 80+: 0.194 | Own estimates from the ISS Covid-19 Surveillance data [68] |
| Reduction factor for hospitalisations among breakthrough infections | 0.3 [0.15, 0.45] | [53] |
| ι_a (proportion of ICU admission among hospitalised) | 0-12: 0.041 13-18: 0.053 19-64: 0.129 65-79: 0.204 80+: 0.104 | Own estimates from the ISS Covid-19 Surveillance data [68] |
| γ_H (non-ICU recovery rate) | 0.067 | Own estimates from the ISS Covid-19 Surveillance data [68] |
| γ_{ICU} (ICU recovery rate) | 0.056 | Own estimates from the ISS Covid-19 Surveillance data [68] |
| γ_{IFR} | 0-12: 0.000016 13-18: 0.00002 19-64: 0.0014 65-79: 0.0198 80+: 0.083 | [61] |

| | | |
|--|---|--|
| α_a (age-specific fatalities/hospitalisations ratio, national averages) | 0-12: 0.004 13-18: 0.006 19-64: 0.075 65-79: 0.315 80+: 0.684 | Own estimates from the ISS Covid-19 Surveillance data [68] |
| First dose efficacy of vaccine group 1 for wild and Alpha variant type | 0.38 [0.29, 0.45] | [53] |
| First dose efficacy of vaccine group 2 for wild and Alpha variant type | 0.37 [0.32, 0.42] | [53] |
| First dose efficacy of vaccine group 1 for Delta type variant | 0.3 [0.17, 0.41] | [53] |
| First dose efficacy of vaccine group 2 for Delta type virus | 0.18 [0.09, 0.25] | [53] |
| Second dose efficacy of vaccine group 1 for wild and Alpha variant type | 0.92 [0.9, 0.93] | [53] |
| Second dose efficacy of vaccine group 2 for wild and Alpha variant type | 0.73 [0.66, 0.78] | [53] |
| Second dose efficacy of vaccine group 1 for Delta type variant | 0.79 [0.75, 0.82] | [53] |
| Second dose efficacy of vaccine group 2 for Delta type virus | 0.6 [0.53, 0.66] | [53] |

Table 2: Parameter values. We report the age-specific parameter when applicable.

A.2. The Tier System in Italy

The classification of geographical entities into zones characterised by different levels of restriction relies on evaluating the epidemic risk in each area and the level of R_t . Regarding the definition of risk, the Italian Ministry of Health elaborated two algorithms in April 2020: the first one to evaluate the probability of a spread (Figure 7), the second one to evaluate its impact (Figure 8). Each algorithm relies on a set of *ad hoc* indicators (21 in total, see Table 3).[67] For both the probability of spread and impact, each algorithm maps the indicators into four different levels: i) very low, ii) low, iii) moderate, iv) high. Then, the joint combination of probability and impact determines the

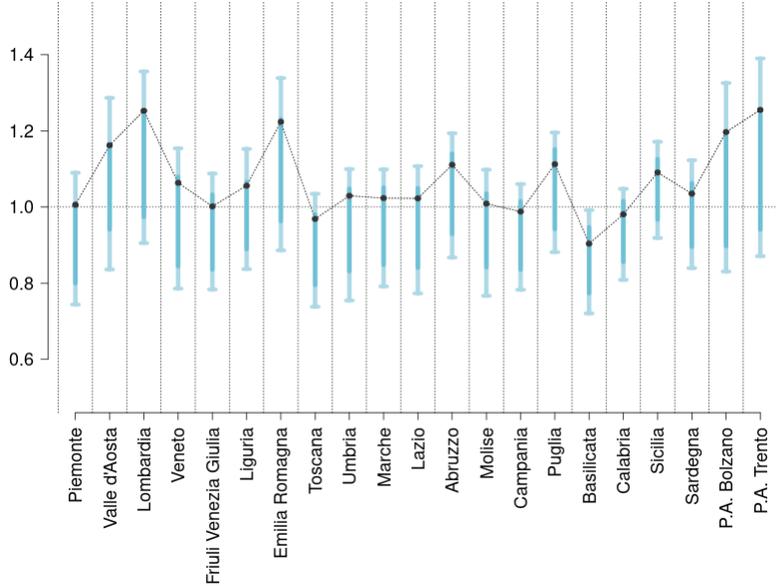


Figure 6: Estimated regional contributions and range of variation for varying temperatures. Light blue bars depict the regional maximum and minimum observed values; darker bars highlight the first and third quartile.

risk of each area according to the scheme contained in Figure 9. Moreover, the indicators 1.1 – 1.6 in Table 3 work as a prerequisite for the quality and reliability of the data used to evaluate the epidemic situation in each region. The other layer to define the policy measures in each geographical entity relied on the level of R_t . In August 2020, the Health Minister defined four scenarios depending on the level of R_t . The four scenarios are the following: i) $R_t < 1$, ii) $1 \leq R_t < 1.25$, iii) $1.25 \leq R_t < 1.5$, iv) $R_t \geq 1.5$.

The decision to enforce a “zone” in a geographical entity hinges on evaluating risk and scenario. The Decree 3 November 2020 defines the zones in the following way:

1. High/Very high risk and Scenario 4 → “Red zone”.
2. High/Very high risk and Scenario 3 → “Orange zone”.
3. Any level of risk and Scenario 1 or 2 → “Yellow zone”.

In January 2021, the Health Minister decided to include an additional indicator based on the incidence in the area and to introduce a “white zone”

for situations in which both low incidence and risk occur (Decree 14 January 2021). Specifically, the incidence is low if weekly cases are less than 50 per 100,000 inhabitants for three consecutive weeks (Figure 9). The Decree 23 February 2021 slightly changed the algorithm in Figure 10. In particular, when incidence is low, the yellow zone also applies if the region is at high risk and R_t is larger than 1.25 (Scenario 3 or 4). Starting from March, the red zone restrictions also trigger if the weekly incidence exceeds 250 cases per 100,000 inhabitants (Decree 13 March 2021).

The decree 18 May 2021 introduced further novelties in the classification of regions. The incidence becomes a crucial parameter. In particular, the decree considers four different levels of incidence: lower than 50 cases per 100,000 inhabitants, lower than 150 cases, lower than 250 cases, above 250 cases. The observed level of incidence, together with the risk, defines the zone assignment of the geographical entity (see Figure 11). The new monitoring system is fully in force starting from 16 June 2021. Until that date, the classification also relied on the old system (see Figure 10), with potential conflicts between the two mechanisms solved by applying the lowest level of restrictions. Finally, on 23 July 2021, the Government issued a new decree to update the criteria for the classification (Decree 23 July 2021). The new criteria mainly use the bed occupancy rate in the hospitals (see Figure 12). In detail, the white zone applies when the weekly incidence is below 50 cases per 100.000 inhabitants for three weeks in a row. Alternatively, it also applies if the ICU occupancy rate is below 10% or the hospital bed occupancy rate is below 15%. When the weekly incidence is between 50 and 150 cases per 100.000 inhabitants and the criteria for the white zones are not met, the yellow zone applies. Alternatively, it also applies if the incidence is above 150 and either ICU occupancy rate is below 20% or hospital bed occupancy rate is below 30%. When the weekly incidence is above 150 cases per 100.000 inhabitants and the criteria for the yellow zone are not met, the orange zone applies if ICU and hospital bed occupancy rates are above 20% and 30%, respectively. When both rates exceed 30% and 40%, respectively and the incidence and the incidence is above 150 cases per 100.000 inhabitants, the red zone applies.

In the model, the assignment of the level of restrictions to a region follows its real-world design closely. The primary difference concerns the absence of the long-term care-associated indicators, as we neglect them in our model.

| Area | Indicator number | Indicator |
|---|------------------|--|
| Monitoring: quality of surveillance systems and data collection | 1.1 | Symptomatic cases per month for which the onset of symptoms is known/Symptomatic cases in the same period |
| | 1.2 | Cases per month requiring hospitalisation (not in ICU) for which the hospitalisation date is known/Cases requiring hospitalisation (not in ICU) in the same period |
| | 1.3 | Cases per month requiring ICU admission for which admission date is known/Cases requiring ICU admission in the same period |
| | 1.4 | Cases per month for which the municipality of residence is known/Cases in the same period |
| | 1.5 (optional) | Share of long-term care facilities that have received the checklist |
| | 1.6 (optional) | Share of long-term care facilities that have reported a critical issue in the checklist |
| Testing capacity | 2.1 | Share of positive tests per month (possibly excluding screening or re-testing of the same individuals) |
| | 2.2 | Delay between symptom onset and date of diagnosis |
| | 2.3 (optional) | Delay between symptom onset and date of isolation |
| Contact-tracing, isolating, quarantine | 2.4 | Number and characteristics of professionals and time dedicated to contact-tracing |
| | 2.5 | Number and characteristics of professionals and time dedicated to testing and monitoring of close contacts |
| | 2.6 | Share of confirmed cases for which contact tracing is carried out |

| | | |
|------------------------------|----------------|--|
| Stability of transmission | 3.1 | Cases reported by the Italian civil protection in the last 14 days |
| | 3.2 | Rt based on symptom onset or hospitalisation date |
| | 3.3 (optional) | Cases reported to a sentinel system (COVID-net) in a week |
| | 3.4 | Daily cases by date of diagnosis and symptom onset |
| | 3.5 | Number of outbreaks (more than 2 linked cases or unexpected increase of cases in a given time and place) |
| | 3.6 | New cases with unknown transmission |
| | 3.7 (optional) | Access to emergency care with symptoms compatible with Covid-19 |
| Health services availability | 3.8 | ICU occupancy rate |
| | 3.9 | Hospital bed occupancy rate |

Table 3: Indicators used by the Italian Ministry of Health for monitoring the epidemic, Decree Ministry of Health 30 April 2020.

A.3. The *Italy Stringency Index*

We construct a new dataset of the measures enforced at the local level in Italian municipalities, provinces, and regions (in total, almost 8,000 municipalities, 107 provinces, including the two autonomous ones, and 19 regions) starting from 1 January 2020.[20] We rely on local laws available through the official websites of regions and local entities. Moreover, we use the information contained in press articles and releases. We enrich the available information set by including the zone assignment of the regions and autonomous provinces enforced by the central Government via the Ministry of Health. The data allow us to compute a national stringency index, the *Italy Stringency Index*, ItSI, as the population-weighted average of the stringency indexes at the subnational level implied by the restrictions.

We re-code some of the variables of the Oxford Stringency Index[32] to

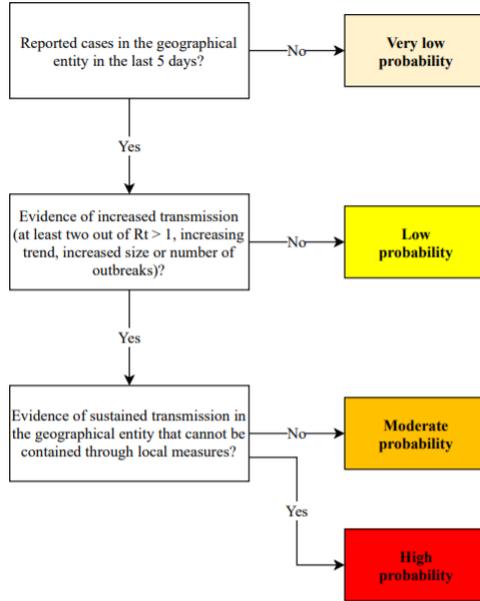


Figure 7: Probability algorithm, Decree Ministry of Health 30 April 2020.

account for the intensity and features of the restrictions adopted in Italy (see Table 4). As in the Oxford Stringency Index, for each region r , we compute a sub-indicator I_j^r of the intensity of the policy measure V_j . In particular, $I_j^r = \frac{v_j^r}{\bar{v}_j^r}$, where v_j^r varies between 0 and \bar{v}_j^r , which is the maximum value that V_j can attain. In the expression, we neglect the time index for ease of notation. We also take into account that some measures were in force only on some days of the week (for example, weekend closures of shops in malls selling non-essential goods or services) or assign intermediate values with respect to those reported in Table 4 to account for in-between cases (for example, due to *ad hoc* provisions at the regional level). Finally, we compute an indicator at the regional level by taking the simple average of the nine available sub-indicators. We disaggregate the indicator relative to “Workplace closing” in three sub-indicators: *i*) Production, *ii*) Shops, *iii*) Bars and restaurants. Then, we collapse the three sub-indicators by a simple average.

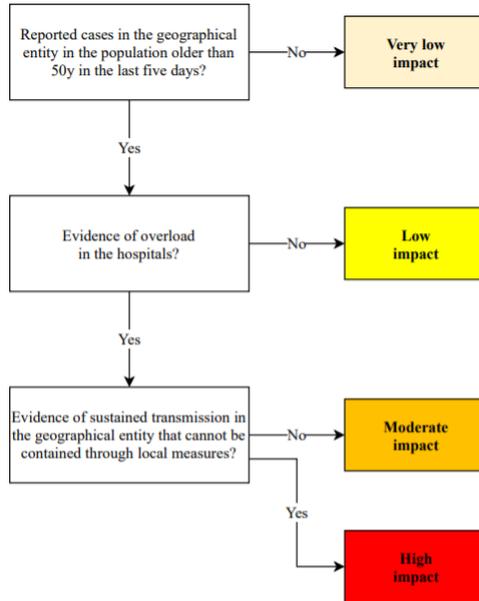


Figure 8: Impact algorithm, Decree Ministry of Health 30 April 2020.

| <i>Probability</i> <i>Impact</i> | Very low | Low | Moderate | High |
|-------------------------------------|---------------|---------------|---------------|----------------|
| Very low | Very low risk | Low risk | Low risk | Moderate risk |
| Low | Low risk | Low risk | Moderate risk | Moderate risk |
| Moderate | Low risk | Moderate risk | Moderate risk | High risk |
| High | Moderate risk | Moderate risk | High risk | Very high risk |

Figure 9: Probability-impact matrix, Decree Ministry of Health 30 April 2020.

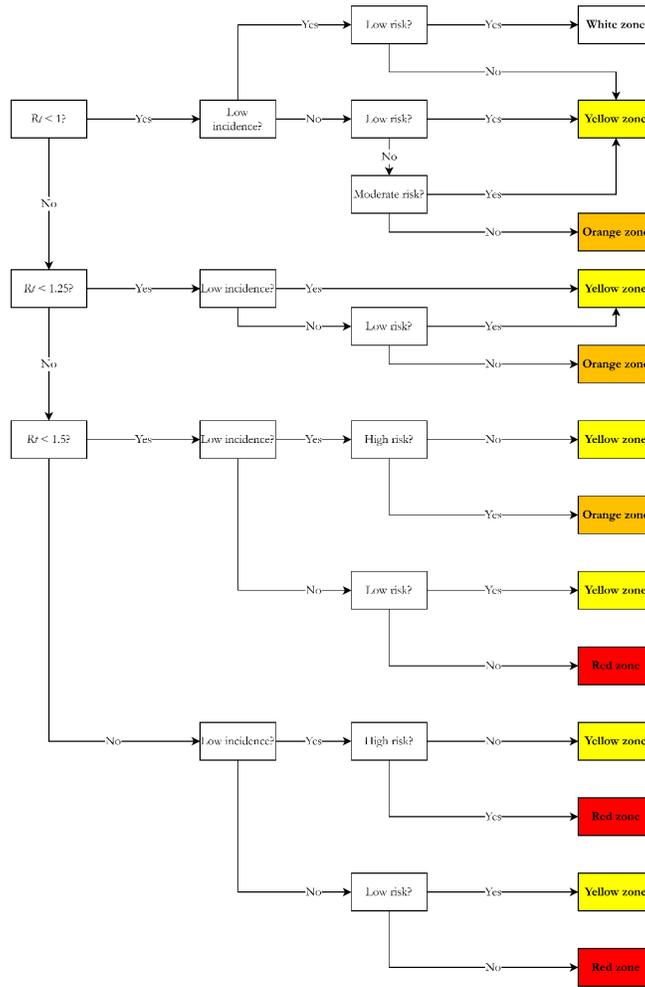


Figure 10: Definition of zones, Decree 14 January 2021. Source: authors' elaboration based on Decree 14 January 2021. The Decree 23 February 2021 slightly changed the algorithm. In particular, when incidence is low, the "Yellow zone" also applies if the region is at high risk and R_t is larger than 1.25 (Scenario 3 or 4).

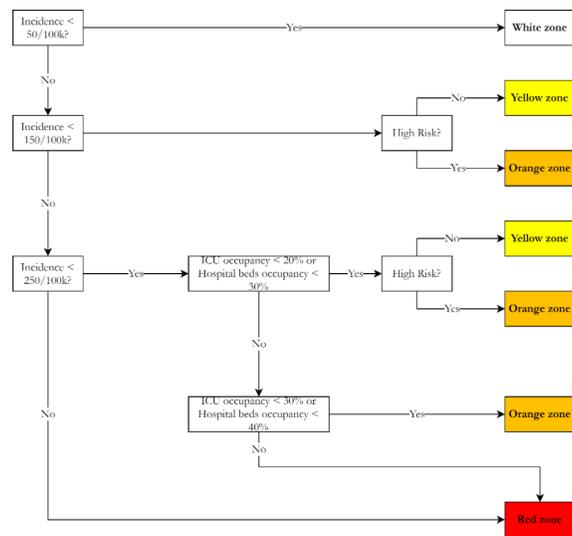


Figure 11: Definition of zones, Decree 18 May 2021.

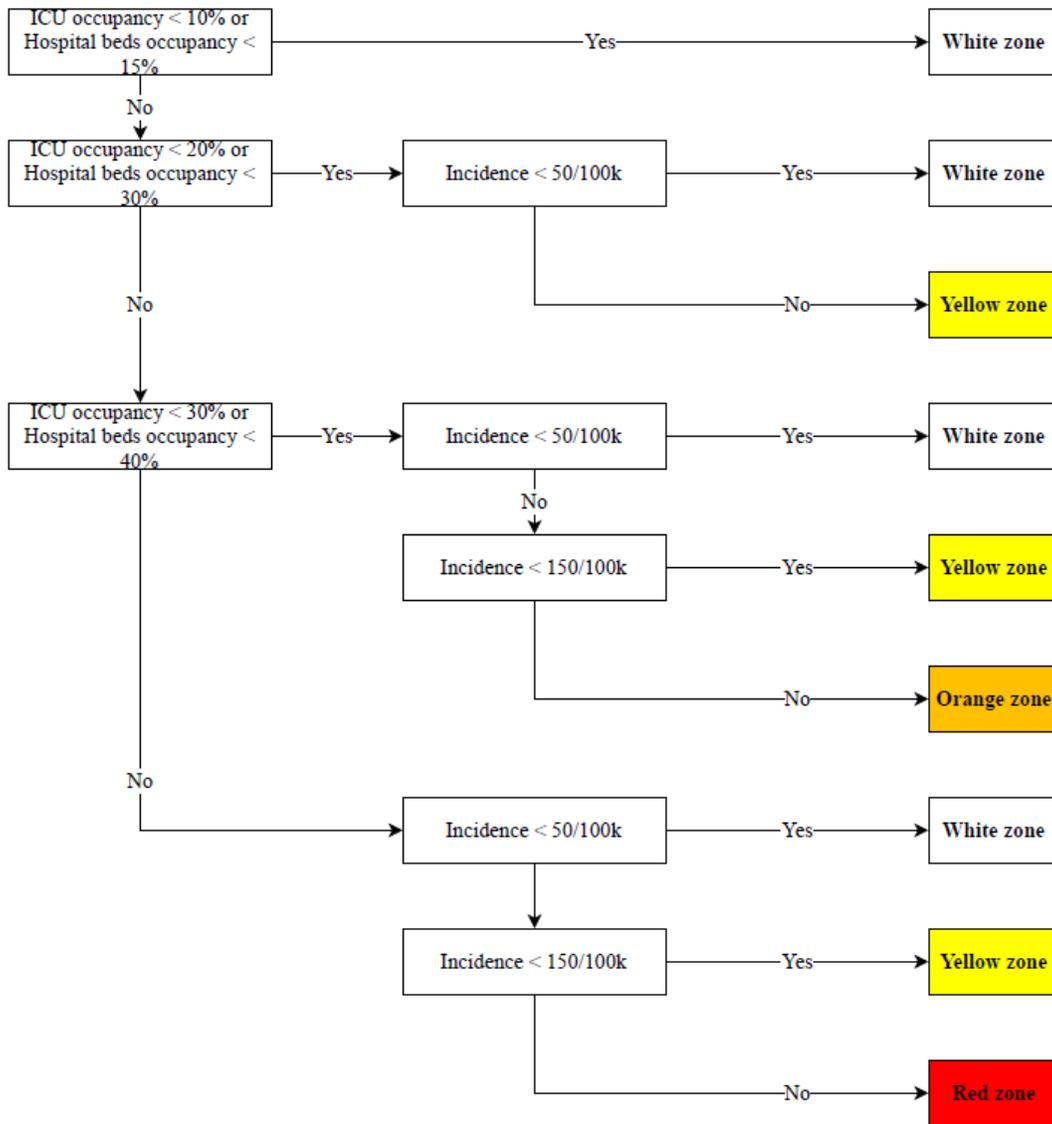


Figure 12: Definition of zones, Decree 23 July 2021.

| Variable | Level | Description | Variable | Level | Description | |
|------------------------------|------------------------|---|-----------------------------|--|---|------------------------------|
| <i>C1_School</i> | 0 | No measures | <i>C4_Gatherings</i> | 0 | No measures | |
| | 0.5 | Limited measures | | 1 | Restrictions on gatherings above 1,000 people | |
| | 1 | Distance education for upper secondary schools | | 2 | Restrictions on gatherings up to 1,000 people | |
| | 1.5 | Distance education for upper secondary schools and second and third grade of lower secondary school | | 3 | Restrictions on gatherings up to 100 people | |
| | 2 | Distance education for upper and lower secondary school | | 4 | Restrictions on gatherings up to 10 people | |
| | 2.5 | Distance education for all schools (except for kindergartens) | | 0 | No measures | |
| | 3 | All school closed or in distance education | | 1 | Limited restrictions | |
| | <i>C2_1_Production</i> | 0 | | No restrictions | 2 | Shutdown of public transport |
| | | 1 | | Recommended work from home | 0 | No measures |
| | | 2 | | Require work from home | 1 | Recommended sheltering |
| <i>C2_2_Shops</i> | 3 | Require closing all-but essential workplaces | 2 | Mandatory sheltering (excluded essential activities) | | |
| | 0 | No measures | 3 | Mandatory sheltering | | |
| | 1 | Limited measures | 0 | No measures | | |
| <i>C2_3_Bars_Restaurants</i> | 2 | Limited closures | 1 | Limited measures (e.g. curfew) | | |
| | 3 | Ban on non-essential products | 2 | No movement between regions | | |
| | 0 | No measures | 3 | No movement between municipalities | | |
| <i>C3_Public_Events</i> | 1 | Dine-in-allowed at some times of the day | 4 | No movement within a municipality | | |
| | 2 | Dine-in not-allowed | 0 | No measures | | |
| | 3 | Require closing | 1 | Require negative test | | |
| <i>C5_Public_transport</i> | 0 | No measures | 2 | Mandatory quarantine | | |
| | 1 | Limited ban on public events | 3 | Entry ban on some countries | | |
| | 2 | Ban on all public events | 4 | Entry ban on all countries | | |
| <i>C6_Stay_at_home</i> | | | <i>C7_Internal_movement</i> | 0 | No measures | |
| | | | | 1 | Public campaign on some media | |
| | | | | 2 | Coordinated campaigns on all media | |

Table 4: Description of the variables used to construct the *Italy Stringency Index*.

A.4. Vaccine Rollout and Coverage Rate Scenarios

Administration rates were determined considering the deliveries of new doses, the administration constraints, the delay between the two injections and the historical data. Up to December 2021, we use historical data on new vaccinations by age group and region provided by the Italian Civil Protection.[42]

For the period December '21 – March '22, we need to make assumptions on the pace of vaccination and booster administration. In particular, in the *Actual rollout*, we assume that only vaccines of type 1 are administered to the population since December in line with the available evidence at the end of November (type 2 vaccines were negligible). We assume an increase in first-dose administration for the last three age groups in December 2021 to fit the fact that accessing the workplace requires either vaccination or a previous infection. In the first quarter of 2022, vaccination campaign continues at a slower pace. We also assume that the vaccination in the youngest cohort takes off in December 2021 and decreases over time in the first quarter of 2022. As far as it concerns the booster administration, we follow the provisions of the Italian Ministry of Health. At the end of September, the third dose was recommended to individuals with a high risk of severe disease, individuals above 80 years old, healthcare workers above 60 years old or at a high risk of severe disease six months after full vaccination. In October, individuals above 60 and all high-risk individuals could access to the third dose. In November and December, the third dose was extended to individuals above 40 and 18, respectively. Moreover, people can get the third dose five months after the full vaccination. Finally, in January, individuals above 12 could access to the third dose four months after the full vaccination. Besides the *Actual rollout*, we also consider an optimistic scenario (*Optimistic rollout*) and a pessimistic one (*Pessimistic rollout*). *Optimistic rollout* assumes a faster rollout than observed between June and November (20% faster in the second and third age groups, 55% for the fourth age group, and 105% faster for the fifth age group). *Pessimistic rollout* assumes a slower rollout than observed (80% of actual doses for all age groups between June and December). *Pessimistic (Optimistic) rollout* shows a faster (slower) reduction of first doses than *Actual rollout* during December 2021-March 2022. *Optimistic (Pessimistic) rollout* assumes a fast (slow) deployment of boosters to the eligible individuals. Moreover, vaccinated individuals may access to boosters after 4 months after the second dose in *Optimistic rollout*. Overall, the allocation of boosters works according to a first-in-first-out principle. In

other words, since we do not have individual-level information on the time span between the vaccinations, we assume that individuals with the older vaccination are the first one to receive a booster. Table 5 reports the average coverage by age-group and scenario at the end of the period (March 2022).

| Age Group | <i>Actual rollout</i> | <i>Optimistic rollout</i> | <i>Pessimistic rollout</i> |
|------------------|-----------------------|---------------------------|----------------------------|
| 0-12 | 39.5% | 55.0% | 20.7% |
| 13-18 | 77.8% | 90.5% | 64.9% |
| 19-64 | 89.7% | 96.8% | 80.2% |
| 65-79 | 97.5% | 99.0% | 91.0% |
| 80+ | 98.3% | 99.4% | 95.0% |

Table 5: Average coverage by age group and scenario.

A.5. Additional Exhibits on the Alpha variant

Counterfactual analysis: assessing the “decoupling” between the United States and Italy

Since the beginning of 2021, the pandemic has shown heterogeneous trends worldwide: while Europe was facing its third wave, in the United States, infections sharply declined, remaining at relatively lower levels until the end of May, despite enforcing less severe restrictions as compared to Europe. In the first quarter of 2021, the Oxford Stringency Index [32] has been about 15 points lower in the United States than in Italy and Germany. As measured by the Google Covid-19 Community Mobility Reports [52], retail and recreation mobility had been gradually growing and approaching pre-pandemic levels by the end of the quarter in the United States, while in Europe, it remained 30%-60% below pre-pandemic levels (see Figure 17).

The different progress of the vaccination campaign has been commonly considered as the main factor behind the observed divergence between epidemic trends in the two regions. Indeed, at the end of the first quarter, in the United States, about 30% of the population had received at least one dose of the vaccine compared to just over 11% in Italy (see Figure 18). In spring, the vaccine rollout accelerated in Europe so that the vaccine gap between the United States and Italy was almost entirely closed by mid-June. Besides vaccine rollout, at least one other factor could have played an essential

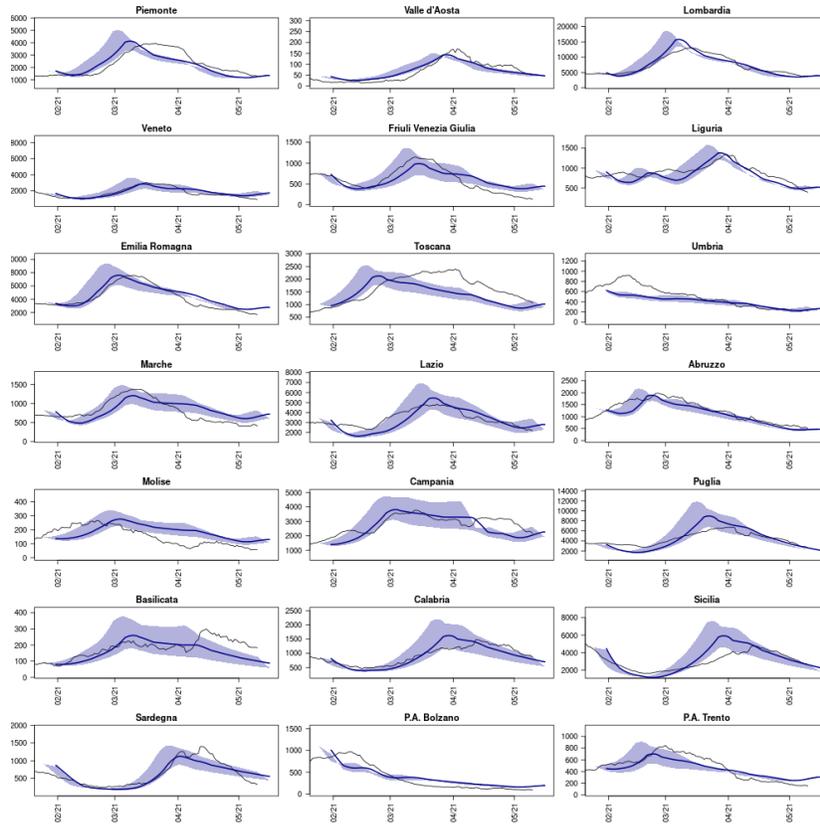


Figure 13: Estimated overall daily incidence. Total number of actual cases with exogenous policy, by region.

role in favouring the decoupling: the different spread of more transmissible SARS-Cov-2 variants. According to the US Centers for Disease and Control and Prevention, the proportion of US cases attributed to the Alpha variant was around 25%-30% in mid-March compared to 87% in Italy [23]. Other things being equal, this would entail a delay of about 5-6 weeks compared to the progress of the same variant in Italy and most other EU countries. It is hard to evaluate the role of different factors just by looking at the evolution of epidemic and restriction dynamics across countries. Many confounding factors such as initial epidemic conditions, demographic characteristics, differences in containment policies and individual behaviours may undermine the possibility of getting a precise evaluation of the contribution of a specific component. By considering the endogenous response of containment poli-

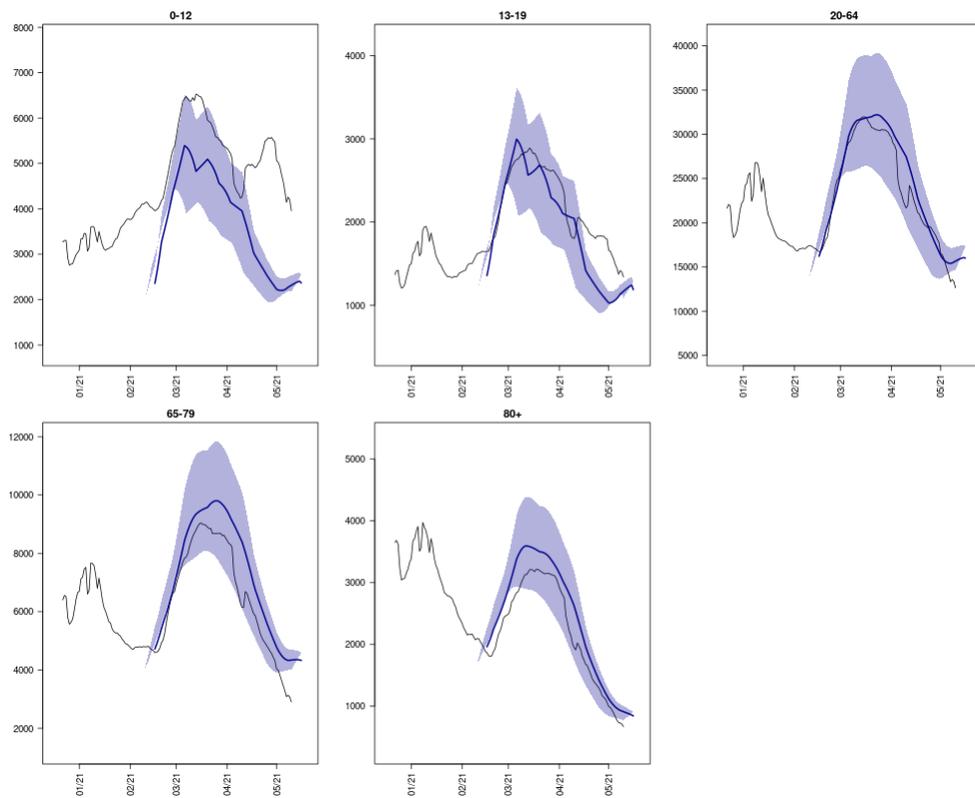


Figure 14: Estimated overall daily incidence by age class.

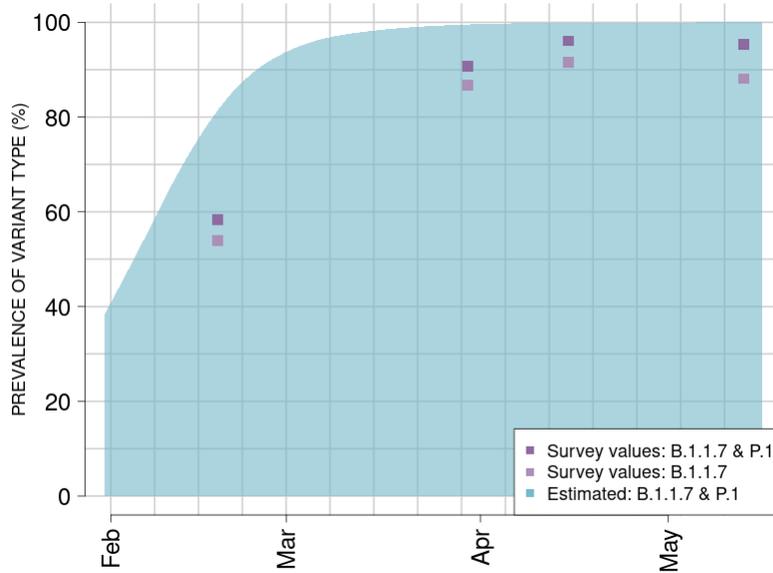


Figure 15: Estimated prevalence of variant types vs Survey values.

cies, our modelling framework may also be a valuable tool to analyse how a specific external factor may affect contagion and restrictions once applied to a specific country (Italy in our case).

To provide a quantitative assessment of how the vaccination progress and the initial prevalence of more transmissible variants may have influenced the divergence between Italy and the United States, we construct two *ad hoc* counterfactual scenarios for February-May 2021. In the counterfactuals, we apply to Italy the more favourable conditions prevailing in the United States regarding the vaccine rollout and the prevalence of more transmissible variants. Clearly, there are other possible sources of divergence, such as the possible differences in the immunity due to previous infections, the general initial incidence of infections. However, we aim to assess how - *ceteris paribus* - the changes in these two specific conditions would have affected epidemic and stringency conditions in Italy. In the first counterfactual scenario, we assume the spread of the Alpha variant to occur in Italy with a delay of 40 days; in the second one, on top of a delayed diffusion of the variant, we consider a vaccine rollout similar to the one in the United States (see Figure 19).

We examine the evolution of the number of notified cases and the modi-

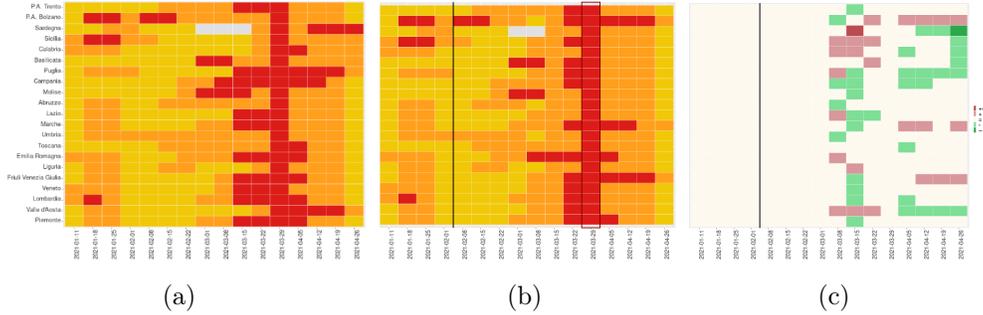


Figure 16: Regional mitigation measures observed and estimated during the third wave. From left to right: observed regional mitigation measures, estimated measures and difference between the two. The colours of the right and middle matrices correspond to the level of weekly restrictions adopted by each region. The white, yellow, orange and red cells correspond to the levels of restrictions prescribed by the tier system. Additionally, the black line highlights the start of the tier estimation exercise, whereas the dark red rectangle indicates exogenous adoption of *ad hoc* enforcement of additional restrictions for the Easter holidays. The rightmost matrix reports the difference between observed and estimated mitigation measures: red shaded cells indicate predicted tiers are more restrictive by one (+) or two (++) notches; e.g., an orange predicted tier for a yellow region corresponds to a pale red cell (+), a predicted red tier for a yellow one corresponds to a dark red cell (++)). Conversely, green cells report on tiers predicted by the model found to be less restrictive than observed ones by one (-) or two (-) notches; e.g., a predicted yellow tier for an observed orange region corresponds to a pale green cell (-), it corresponds to a dark green cell in the matrix for a red region (-). Finally, white cells represent equal tiers (=).

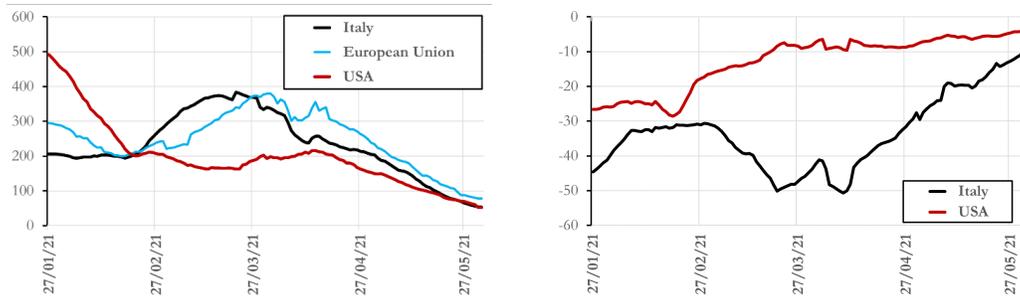


Figure 17: Epidemic and mobility in the US and Italy. [70, 52]

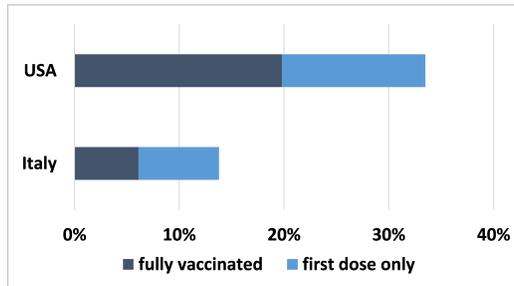


Figure 18: Share of people who received at least one dose of Covid-19 vaccine in the United States and Italy. Source: Our World in Data.

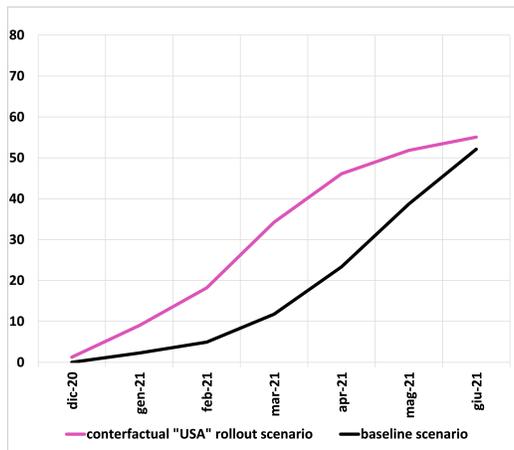


Figure 19: Vaccine rollout scenarios: share of total population covered.

fied version of the Oxford Stringency Index in these two alternative scenarios, comparing them with the realised dynamics (Figure 20). As for the latter, we consider the values produced by simulations instead of actual data so that any difference in the counterfactual scenarios can be attributed only to the variation of external conditions instead of model deviations from actual data. Nevertheless, results would not substantially change when using realised data, given the model’s ability to track actual evolutions over the considered period (see Figure 7 in Section 4).

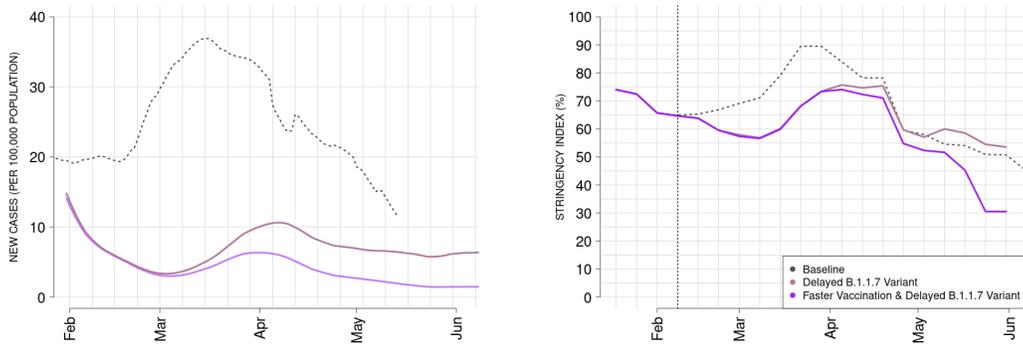


Figure 20: Simulated dynamic of Oxford Stringency index for Italy: counterfactual scenarios.

The simulations suggest that the main driver for the divergence in February-March was the early diffusion of the Alpha variant in Italy, which is associated with an average increase of 72.5% in notified cases and of 8.5 points in the Oxford Stringency Index (compare the dashed and brown lines in Figure 20). After realigning the spread of the Alpha variant, a faster vaccination campaign becomes the leading factor (compare the brown and purple lines). In particular, a rapid vaccine rollout leads to an average reduction of 56.5% in notified cases and of 7.7 points in the Oxford Stringency Index in April-May. Considering the entire simulation period, a delayed diffusion of the new variants accounts for about 60.0% in moderating the number of new cases and - on average - for about 7.8 points in reducing the level of restrictions. A faster vaccine rollout would have allowed a further relaxation of the policies, by additional 3.6 points on average, while the number of cases would have fallen by an additional 13.3%. These results point out the importance of preventing or delaying the spread of insidious variants of the virus during the vaccination campaign.

A.6 Fixed restrictions vs. self-adaptive rule-based mechanism

Figure 21 displays the counterfactual scenarios in which “yellow”, “orange”, and “red” zone restrictions apply to the national territory during the whole simulation period. In this way, we can compare the results of our modelling framework with those of an epidemiological model that does not embed endogenous adjustments of the containment measures. The left panel of Figure 21 shows the projections for new cases associated with each regime (“yellow”, “orange”, and “red”). As one may expect, we observe that the severity and the length of the epidemic wave are inversely related to the restrictiveness of the policies. While a nationwide red zone allows a rapid suppression of the epidemic by the end of the spring, the yellow zone determines a substantial increase of cases until April and a slow reduction until May. The lack of an endogenous adjustment policy mechanism clearly translates into a large epidemic burden (the yellow-zone policy) or disproportionate restrictions (the red-zone policy). Moreover, constant policies do not reflect dynamically the progress of the vaccination campaign, which allows the policymakers to reduce restrictions and the epidemic burden at the same time. Finally, the right panel of Figure 21 shows that the level of restrictions associated with an unconditional application of red and orange zones would be much larger than the self-adaptive policy mechanism described in this paper. On the contrary, the constant application of the yellow zone would result in too lenient restrictions.

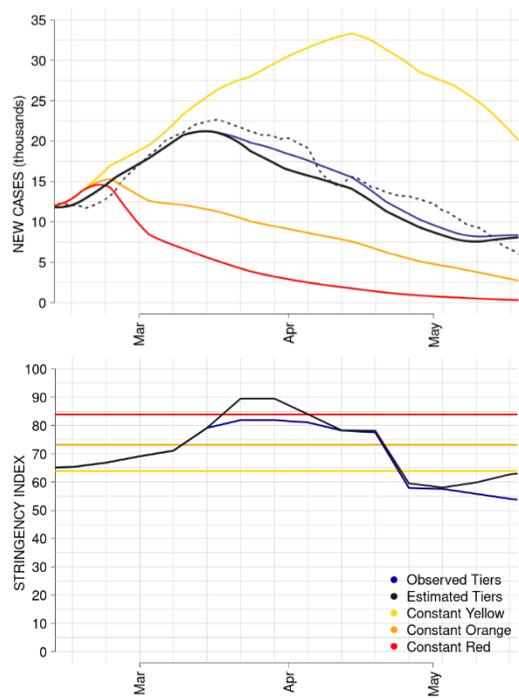


Figure 21: New cases and the Italy Stringency Index during the third wave. The dashed curve in the left panel reports the observed new cases.

References

- [1] J. Abaluck et al. “Impact of community masking on Covid-19:A cluster-randomized trial in Bangladesh”. In: *Science* 375 (6577 2022). DOI: <http://doi.org/10.1126/science.abi9069>.
- [2] D. Acemoglu et al. “Optimal Targeted Lockdowns in a Multigroup SIR Model”. In: *American Economic Review: Insights* 3 (4 2021), pp. 487–502. DOI: <https://doi.org/10.1257/aeri.20200590>.
- [3] J. V. Alipour, H. Fadinger, and J. Schymik. “My home is my castle - The benefits of working from home during a pandemic crisis”. In: *Journal of Public Economics* 196 (2021). DOI: <https://doi.org/10.1016/j.jpubeco.2021.104373>.
- [4] F. Alvarez, D. Argente, and F. Lippi. “A Simple Planning Problem for Covid-19 Lockdown, Testing, and Tracing”. In: *American Economic Review: Insights* 3 (3 2021), pp. 367–382. DOI: <https://doi.org/10.1257/aeri.20200201>.
- [5] Elena Angelini et al. *ECB-BASIR: a primer on the macroeconomic implications of the Covid-19 pandemic*. Preprint available at <https://www.ecb.europa.eu/pub/pdf/scpwps/ecb.wp2431~aab2650200.en.pdf>. 2020.
- [6] Valentina Aprigliano et al. *Forecasting Italian GDP growth with epidemiological data*. Questioni di Economia e Finanza (Occasional Papers) 664. Bank of Italy, Economic Research and International Relations Area, 2021. URL: https://EconPapers.repec.org/RePEc:bdi:opques:qef_664_21.
- [7] K. A. Auger et al. “Association Between Statewide School Closure and Covid-19 Incidence and Mortality in the US”. In: *JAMA* 324 (9 2020), pp. 859–870. DOI: <https://doi:10.1001/jama.2020.14348>.
- [8] T. Barbieri, G. Basso, and S. Scicchitano. “Italian workers at Risk During the Covid-19 Epidemic”. In: *Ital Econ J* (2021). DOI: <https://doi.org/10.1007/s40797-021-00164-1>.
- [9] Elena Bobeica and Benny Hartwig. “The Covid-19 shock and challenges for inflation modelling”. In: *International journal of forecasting* (2022). DOI: <https://doi.org/10.1016/j.ijforecast.2022.01.002>.

- [10] Martin Bodenstein, Giancarlo Corsetti, and Luca Guerrieri. *Social distancing and supply disruptions in a pandemic*. Preprint available at <https://www.federalreserve.gov/econres/feds/social-distancing-and-supply-disruptions-in-a-pandemic.htm>. 2020. DOI: <https://doi.org/10.17016/FEDS.2020.031>.
- [11] A. Brodeur et al. “Covid-19, lockdowns and well-being: Evidence from Google Trends”. In: *Journal of Public Economics* 193.104346 (2021). DOI: <https://doi.org/10.1016/j.jpubeco.2020.104346>.
- [12] Michal Brzoza-Brzezina, Marcin Kolasa, and Krzysztof Makarski. *Monetary policy and Covid-19*. Preprint available at https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4026503. 2021. DOI: <https://dx.doi.org/10.2139/ssrn.4026503>.
- [13] W. S. Byun et al. “Is coronavirus disease (Covid-19) seasonal? A critical analysis of empirical and epidemiological studies at global and local scales”. In: *Environmental Research* 196.110972 (2021). DOI: <https://doi.org/10.1016/j.envres.2021.110972>.
- [14] Cem Çakmaklı et al. *The economic case for global vaccinations: an epidemiological model with international production networks*. Tech. rep. National Bureau of Economic Research, 2021.
- [15] Andrea Carriero et al. *Measuring uncertainty and its effects in the Covid-19 era*. Preprint available at https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3717973. 2020. DOI: <https://dx.doi.org/10.2139/ssrn.3717973>.
- [16] F. Caselli et al. “The Great Lockdown: Dissecting the Economic Effects”. In: *World Economic Outlook, October 2020*. International Monetary Fund, 2020, pp. 65–84. DOI: <https://doi.org/10.5089/9781513556055.081.ch002>.
- [17] V. Chernozhukov, H. Kasahara, and P. Schrimpf. “Causal impact of masks, policies, behavior on early Covid-19 pandemic in the U.S.” In: *Journal of Econometrics* 220 (1 2021), pp. 23–62. DOI: <https://doi.org/10.1016/j.jeconom.2020.09.003>.
- [18] R. Chetty et al. *The Economic Impacts of Covid-19: Evidence from a New Public Database Built Using Private Sector Data*. Preprint at NBER <https://www.nber.org/papers/w27431>. 2020. DOI: <https://doi.org/10.3386/w27431>.

- [19] Coibion, O. and Gorodnichenko, Y. and Weber, M. *The Cost of the Covid-19 Crisis: Lockdowns, Macroeconomic Expectations, and Consumer Spending*. Preprint at <https://www.nber.org/papers/w27141>. 2020. DOI: <https://doi.org/10.3386/w27141>.
- [20] F. P. Conteduca and A. Borin. *A new dataset for local and national Covid-19-related restrictions in Italy*. Preprint at SSRN https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4023312. 2021.
- [21] Michael E Darden et al. *Modeling to Inform Economy-Wide Pandemic Policy: Bringing Epidemiologists and Economists Together*. Preprint available at <https://www.nber.org/papers/w29475>. 2021.
- [22] Di Domenico, L. and Pullano, G. and Sabbatini, C. E. and Boëlle, P. Y. and Colizza, V. “Impact of lockdown on Covid-19 epidemic in Île-de-France and possible exit strategies”. In: *BMC Medicine* 18 (240 2020). DOI: <https://doi.org/10.1186/s12916-020-01698-4>.
- [23] Centers for Disease Control and Prevention. *Variant Proportions*. Centers for Disease Control and Prevention. Available at <https://covid.cdc.gov/covid-data-tracker/#variant-proportions>. 2021.
- [24] I. Dorigatti et al. “SARS-CoV-2 antibody dynamics and transmission from community-wide serological testing in the Italian municipality of Vo”. In: *Nat Commun* 12.4383 (2021). DOI: <https://doi.org/10.1038/s41467-021-24622-7>.
- [25] Martin S Eichenbaum, Sergio Rebelo, and Mathias Trabandt. *The macroeconomics of testing and quarantining*. Preprint available at <https://www.nber.org/papers/w27104>. 2020. DOI: <https://doi.org/10.3386/w27104>.
- [26] P. D. Fajgelbaum et al. “Optimal Lockdown in a Commuting Network”. In: *American Economic Review: Insights* 3 (4 2021), pp. 503–522. DOI: <https://doi.org/10.1257/aeri.20200401>.
- [27] Matthew Famiglietti and Fernando Leibold. *The impact of health and economic policies on the spread of Covid-19 and economic activity*. Preprint available at https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3843874. 2021. DOI: <https://dx.doi.org/10.20955/wp.2021.005>.

- [28] S. Flaxman et al. “Estimating the effects of non-pharmaceutical interventions on Covid-19 in Europe”. In: *Nature* 584 (2020), pp. 257–261. DOI: <https://doi.org/10.1038/s41586-020-2405-7>.
- [29] Y. Goldberg et al. “Waning Immunity after the BNT162b2 Vaccine in Israel”. In: *N Engl J Med* 385 (e85 2021). DOI: <https://doi.org/10.1056/NEJMoa2114228>.
- [30] A. Goolsbee and C. Syverson. “Fear, lockdown, and diversion: Comparing drivers of pandemic economic decline”. In: *Journal of Public Economics* 193.104311 (2021). DOI: <https://doi.org/10.1016/j.jpubeco.2020.104311>.
- [31] Gourinchas, P. and Kalemli-Özcan, S. and Penciakova, V. and Sander, N. *Estimating SME Failures in Real Time: An Application to the Covid-19 Crisis*. Preprint at CEPR https://cepr.org/active/publications/discussion_papers/dp.php?dpno=15323. 2022.
- [32] T. Hale et al. “A global panel database of pandemic policies (Oxford Covid-19 Government Response Tracker)”. In: *Nat Hum Behav* 5 (2021), pp. 529–538. DOI: <https://doi.org/10.1038/s41562-021-01079-8>.
- [33] J. Howard et al. “An evidence review of face masks against Covid-19”. In: *Proceedings of the National Academy of Sciences* 118 (4 2021). DOI: <https://doi.org/10.1073/pnas.2014564118>.
- [34] S. Hsiang et al. “The effect of large-scale anti-contagion policies on the Covid-19 pandemic”. In: *Nature* 584 (2020), pp. 262–267. DOI: <https://doi.org/10.1038/s41586-020-2404-8>.
- [35] S. Hu et al. “Infectivity, susceptibility, and risk factors associated with SARS-CoV-2 transmission under intensive contact tracing in Hunan, China.” In: *Nat Commun* 12.1533 (2021). DOI: <https://doi.org/10.1038/s41467-021-21710-6>.
- [36] Bundesministerium des Innern und für Heimat. *Die “Corona-Notbremse” ist bundesweit in Kraft getreten*. Available at <https://www.bmi.bund.de/SharedDocs/textbaustein/DE/service/buergerservice/corona-notbremse.html>. 2021.

- [37] Istituto Superiore di Sanità. *Prevalenza delle varianti VOC (Variant Of Concern) in Italia: lineage B.1.1.7, P.1, P.2, lineage B.1.351, lineage B.1.525 (Indagine del 18/3/2021)*. Available at <https://www.iss.it/documents/20126/0/Rapporto+indagine+varianti+SARS-CoV-2.pdf/3ba8d61d-eeb2-4db2-c33f-250226fa73a7?t=1617126797042>. 2021.
- [38] Istituto Superiore di Sanità. *Prevalenza delle varianti VOC 202012/01 (lineage B.1.1.7), P.1, e 501.V2 (lineage B.1.351) in Italia (Indagine del 18 febbraio 2021)*. Available at <https://www.iss.it/documents/20126/0/Relazione+tecnica+terza+indagine+flash+per+le+varianti+del+virus+SARS-CoV-2+%28%29.pdf/a03f33e6-d775-9ab0-b0ce-9cdd289c711d?t=1614710805598>. 2021.
- [39] Istituto Superiore di Sanità. *Prevalenza delle VOC (Variant Of Concern) del virus SARS-CoV-2 in Italia: lineage B.1.1.7, P.1 e B.1.351, e altre varianti (Variant Of Interest, VOI) tra cui lineage P.2 e lineage B.1.525 (Indagine del 20/4/2021)*. Available at <https://www.iss.it/documents/20126/0/Relazione+tecnica+indagine+rapida+varianti+SARS-CoV-2.pdf/f425e647-efdb-3f8c-2f86-87379d56ce8d?t=1620239550272>. 2021.
- [40] Istituto Superiore di Sanità. *Stima della prevalenza delle varianti VOC (Variants of Concern) in Italia: B.1.1.7, B.1.351, P.1 e B.1.617.2, e altre varianti di SARS-CoV-2 (Indagine del 20/7/2021)*. Available at https://www.iss.it/documents/20126/0/FLASH+SURVEY+Varianti_SARS-CoV-2_30luglio.pdf/6c1c9969-e62c-cf19-6d1e-d9679e21692a?t=1627655177533. 2021.
- [41] Istituto Superiore di Sanità. *Stima della prevalenza delle varianti VOC (Variants of Concern) in Italia: B.1.1.7, B.1.351, P.1 e B.1.617.2, e altre varianti di SARS-CoV-2 (indagine del 22/6/2021)*. Available at <https://www.iss.it/documents/20126/0/FLASH+SURVEY+Varianti++SARS-CoV-2+GIUGNO+2021.pdf/04145998-760b-7a70-ed33-6599369d42cc?t=1625243207797>. 2021.
- [42] Italian Civil Protection. *Covid-19 Opendata Vaccini*. Italian Civil Protection. Available at <https://github.com/italia/covid19-opendata-vaccini>. 2022.

- [43] Italian Ministry of Health. *Circular Ministry of Health, 27 September 2021*. Available at <https://www.trovanorme.salute.gov.it/norme/renderNormsanPdf?anno=2021&codLeg=82953&parte=1\%20\&serie=null>. 2021.
- [44] Italian Ministry of Health. *Circular Ministry of Health, 27 September 2021*. Available at <https://www.trovanorme.salute.gov.it/norme/renderNormsanPdf?anno=2021&codLeg=84033&parte=1\%20\&serie=null>. 2021.
- [45] Italian Ministry of Health. *Circular Ministry of Health, 27 September 2021*. Available at <https://www.trovanorme.salute.gov.it/norme/renderNormsanPdf?anno=2021&codLeg=84679&parte=1\%20\&serie=null>. 2021.
- [46] X. Jaravel and M. O’Connell. “Real-time price indices: Inflation spike and falling product variety during the Great Lockdown”. In: *Journal of Public Economics* 191.104270 (2020). DOI: <https://doi.org/10.1016/j.jpubeco.2020.104270>.
- [47] W. O. Kermack and A. G. McKendrick. “A contribution to the mathematical theory of epidemics”. In: *Proc. R. Soc. Lond.* 115 (1927), pp. 700–721. DOI: <https://doi.org/10.1098/rspa.1927.0118>.
- [48] Michele Lenza and Giorgio E Primiceri. *How to Estimate a VAR after March 2020*. Preprint at NBER <https://www.nber.org/papers/w27771>. 2020. DOI: <https://doi.org/10.3386/w27771>.
- [49] E. G. Levin et al. “Waning Immune Humoral Response to BNT162b2 Covid-19 Vaccine over 6 Months”. In: *N Engl J Med* 385 (e84 2021). DOI: <https://doi.org/10.1056/NEJMoa2114583>.
- [50] N. M. Linton et al. “Incubation Period and Other Epidemiological Characteristics of 2019 Novel Coronavirus Infections with Right Truncation: A Statistical Analysis of Publicly Available Case Data”. In: *Journal of clinical medicine* 9 (2020). DOI: <https://doi.org/10.3390/jcm9020538>.
- [51] Q. H. Liu et al. “Model-based evaluation of alternative reactive class closure strategies against Covid-19”. In: *Nat Commun* 13 (322 2022). DOI: <https://doi.org/10.1038/s41467-021-27939-5>.

- [52] Google LLC. *Google Covid-19 Community Mobility Reports*. Google LLC. Available at <https://www.google.com/covid19/mobility/>. 2022.
- [53] J. Lopez Bernal et al. “Effectiveness of Covid-19 Vaccines against the B.1.617.2 (Delta) Variant”. In: *N Engl J Med* 385 (2021), pp. 585–594. DOI: <https://doi.org/10.1056/NEJMoa2108891>.
- [54] P. Majumder and P.P. Ray. “A systematic review and meta-analysis on correlation of weather with Covid-19”. In: *Sci Rep* 11.10746 (2021). DOI: <https://doi.org/10.1038/s41598-021-90300-9>.
- [55] V. Marziano et al. “The effect of Covid-19 vaccination in Italy and perspectives for living with the virus”. In: *Nature Communications* 12.7272 (2021). DOI: <https://doi.org/10.1038/s41467-021-27532-w>.
- [56] D. McAdams. “The Blossoming of Economic Epidemiology”. In: *Annual Review of Economics* 13 (2021), pp. 539–570. DOI: <https://doi.org/10.1146/annurev-economics-082120-122900>.
- [57] A. Mellone, Z. Gong, and G. Scarciotti. “Modelling, prediction and design of Covid-19 lockdowns by stringency and duration”. In: *Scientific Reports* 11.15708 (2021). DOI: <https://doi.org/10.1038/s41598-021-95163-8>.
- [58] S. M. Moghadas et al. “The Impact of Vaccination on Coronavirus Disease 2019 (Covid-19) Outbreaks in the United States”. In: *Clinical Infectious Diseases* 73 (12 2021), pp. 2257–2264. DOI: <https://doi.org/10.1093/cid/ciab079>.
- [59] S. Moore et al. “Vaccination and non-pharmaceutical interventions for Covid-19: a mathematical modelling study”. In: *Lancet Infectious Diseases* 21 (6 2021), pp. 793–802. DOI: [https://doi.org/10.1016/S1473-3099\(21\)00143-2](https://doi.org/10.1016/S1473-3099(21)00143-2).
- [60] J. Mossong et al. “Social Contacts and Mixing Patterns Relevant to the Spread of Infectious Diseases”. In: *PLoS Med* 5(3): e74 (2008). DOI: <https://doi.org/10.1371/journal.pmed.0050074>.
- [61] M. O’Driscoll et al. “Age-specific mortality and immunity patterns of SARS-CoV-2”. In: *Nature* 590 (2021), pp. 140–145. DOI: <https://doi.org/10.1038/s41586-020-2918-0>.

- [62] M. Oliu-Barton et al. *The effect of Covid certificates on vaccine uptake, health outcomes, and the economy*. Preprint at <https://www.researchsquare.com/article/rs-1242919/v2>. 2022. DOI: <https://doi.org/10.21203/rs.3.rs-1242919/v2>.
- [63] T. Oraby et al. “Modeling the effect of lockdown timing as a Covid-19 control measure in countries with differing social contacts”. In: *Scientific Reports* 11.3354 (2021). DOI: <https://doi.org/10.1038/s41598-021-82873-2>.
- [64] A. L. Phelan. *Covid-19 immunity passports and vaccination certificates: scientific, equitable, and legal challenges*. 2020. DOI: [https://doi.org/10.1016/S0140-6736\(20\)31034-5](https://doi.org/10.1016/S0140-6736(20)31034-5).
- [65] Public Health England. *SARS-CoV-2 variants of concern and variants under investigation in England - Technical briefing 15*. Available at https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/993879/Variants_of_Concern_VOC_Technical_Briefing_15.pdf. 2021.
- [66] Vie Publique. *Zones rouges, carte de vigilance... L'évolution des indicateurs de suivi du Covid-19*. Available at <https://www.vie-publique.fr/en-bref/276020-zones-rouges-carte-de-vigilance-levolution-des-indicateurs-covid-19>. 2020.
- [67] F. Riccardo et al. *Data for action in Covid-19 response: effectiveness of weekly rapid risk assessments in Italy*. 2021. DOI: <https://doi.org/10.5281/zenodo.5638454>.
- [68] F. Riccardo et al. “Epidemiological characteristics of Covid-19 cases and estimates of the reproductive numbers 1 month into the epidemic, Italy, 28 January to 31 March 2020”. In: *Euro Surveill* 25 (49 2020). DOI: <https://doi.org/10.2807/1560-7917.ES.2020.25.49.2000790>.
- [69] K. Rice et al. “Effect of school closures on mortality from coronavirus disease 2019: old and new predictions”. In: *BMJ* 371 (2020). DOI: <https://doi.org/10.1136/bmj.m3588>.
- [70] H. Ritchie et al. *Coronavirus Pandemic (Covid-19)*. Our World in Data. Available at <https://ourworldindata.org/coronavirus>. 2022.
- [71] Phurichai Rungcharoenkitkul. *Macroeconomic consequences of pandexit*. Preprint available at <https://www.bis.org/publ/work932.htm>. 2021.

- [72] A. Sheikh et al. “SARS-CoV-2 Delta VOC in Scotland: demographics, risk of hospital admission, and vaccine effectiveness”. In: *The Lancet* 397 (10293 2021), pp. 2461–2462. DOI: [https://doi.org/10.1016/S0140-6736\(21\)01358-1](https://doi.org/10.1016/S0140-6736(21)01358-1).
- [73] M. A. Shiraef et al. “Did border closures sow SARS-CoV-2?”. In: *Scientific Reports* 12.1709 (2022). DOI: <https://doi.org/10.1038/s41598-022-05482-7>.
- [74] S. Y. Tartof et al. “Effectiveness of mRNA BNT162b2 Covid-19 vaccine up to 6 months in a large integrated health system in the USA: a retrospective cohort study”. In: *The Lancet* 398 (10309 2021), pp. 1407–1416. DOI: [https://doi.org/10.1016/S0140-6736\(21\)02183-8](https://doi.org/10.1016/S0140-6736(21)02183-8).
- [75] UK Government. *Full list of local restriction tiers by area*. Available at <https://www.gov.uk/guidance/full-list-of-local-restriction-tiers-by-area>. 2020.
- [76] E. Vasileiou et al. “Interim findings from first-dose mass Covid-19 vaccination roll-out and Covid-19 hospital admissions in Scotland: a national prospective cohort study”. In: *The Lancet* 397 (10285 2021), pp. 1646–1657. DOI: [https://doi.org/10.1016/S0140-6736\(21\)00677-2](https://doi.org/10.1016/S0140-6736(21)00677-2).
- [77] R. M. Viner et al. “School closure and management practices during coronavirus outbreaks including Covid-19: a rapid systematic review”. In: *Lancet Child & Adolescent Health* 4 (5 2020), pp. 397–404. DOI: [https://doi.org/10.1016/S2352-4642\(20\)30095-X](https://doi.org/10.1016/S2352-4642(20)30095-X).