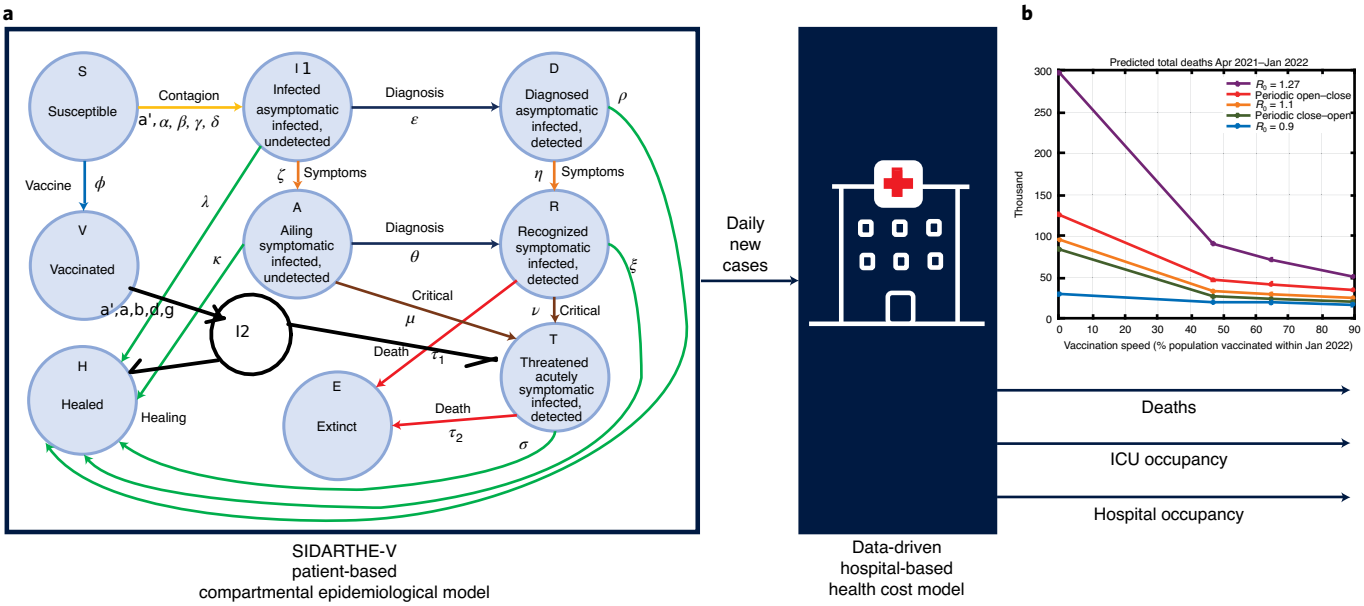

a= alpha, b= beta, d= delta, g=gamma. a' or alpha prime is the transmission rate due to contacts with vaccinated but infected individuals. (I2).

Fig. 1 | Model scheme and summary of our findings. a, Graphical scheme of our model (adapted from Giordano et al.[2]). The compartmental SIDARTHE-V epidemiological model provides daily new cases as an input to a novel data-based model of casualties and healthcare system costs. The SIDARTHE-V model captures the dynamic interactions among nine mutually exclusive infection stages in the population: S, Susceptible (uninfected); I, Infected (asymptomatic infected, undetected); D, Diagnosed (asymptomatic infected, detected); A, Ailing (symptomatic infected, undetected); R, Recognized (symptomatic infected, detected); T, Threatened (infected with life-threatening symptoms, detected); H, Healed (recovered); E, Extinct (dead); and V, Vaccinated (successfully immunized). The SIDARTHE-V model provides the time evolution of daily new infection cases, based on which the data-driven model computes the evolution of deaths and ICU and hospital occupancy. **b**, Death versus vaccination speed curves. For a given $\mathcal{R}_0$ profile, the curve gives the death toll in the period from April 2021 to January 2022 as a function of the average vaccination speed, measured as the fraction of vaccinated population at the end of the period. The death versus vaccination speed curves corresponding to a constant reproduction number are reported in purple ($\mathcal{R}_0 = 1.27$), orange ($\mathcal{R}_0 = 1.1$) and blue ($\mathcal{R}_0 = 0.9$), whereas those corresponding to intermittent strategies are reported in red (Open–Close) and green (Close–Open).

of vaccination becomes more important with a higher $\mathcal{R}_0$, at the price of many more deaths. In Extended Data Figs. 6 and 7, we also consider an adaptive vaccination scenario, where an increase in the number of current infection cases leads to a reduction of the vaccination rate, due to the augmented strain on the healthcare system. Both mortality and healthcare system costs increase, reinforcing conclusions about the greater importance of containment measures over vaccination rates.

There are limitations to our study. The SIDARTHE-V model is a mean-field compartmental model, which relies on the assumption of a large population with homogeneous mixing and provides predictions that are averaged over the whole population; hence, geographical heterogeneity is not taken into account. More complex and detailed models, which account for spatial effects, social networks and the specificity of individual behaviors, can be developed and used to evaluate vaccination strategies[31]. Also, we assumed that vaccination is effective against SARS-CoV-2 variants. However, several concerns are raised regarding variants and their potential for vaccine-induced immunity escape[32,33]; preliminary reports suggest that some COVID-19 vaccines might retain efficacy against variants[34,35], although it might be attenuated[36], whereas data suggest that Oxford–AstraZeneca AZD1222 might be less effective against B.1.351 (ref. [37]). In our scenarios, we also optimistically assumed that successfully vaccinated individuals gain protection against death and hospitalization starting 3 weeks after the first vaccine dose rather than after the second dose.

Vaccination started with slow rates, and priority was given to healthcare personnel, thus delaying the CFR decrease: even under the fast rollout, the CFR would not be halved before June (Extended Data Fig. 4c). Because the decrease rate of the CFR cannot be made arbitrarily fast, due to availability and administration rate of vaccines, our findings confirm that, in the first phase of the mass vaccination campaign, NPIs are crucial, regardless of the (realistic) vaccination speed. Given the circulation of highly transmissible SARS-CoV-2 variants and the risk of potential emergence of vaccine-resistant mutations, $\mathcal{R}_0$ must be kept low until a sufficient level of population immunity is achieved and a large enough portion of the vulnerable population has been immunized. Only then can NPIs be safely and gradually released; the time at which this happens will depend on the speed of vaccine rollout.

To outrun the faster spread of the virus variants, the United Kingdom (UK) launched an extensive COVID-19 vaccination campaign, accelerated by extending the interval between doses: more than 29 million people have received at least one vaccine dose as of 25 March, which has reduced deaths and hospital admissions[38]. Our model confirms that implementation of strong NPIs could bring the epidemic under control without vaccines or before reaching population immunity, as happened in the UK during January 2021: the highly transmissible B.1.1.7 variant, which first emerged in Kent, UK, and spread throughout the UK, was brought under control by lockdown restrictions kept in place during the first crucial phases of the vaccine rollout campaign. In the meantime, vaccine rollout in the UK has enabled planning subsequent gradual release of NPIs[38,39]. Although the UK is heading into the second phase of the vaccination campaign, Italy is at an early phase, close to the UK's first. To contain the new Italian outbreak of SARS-CoV-2, driven by the new variants of concern, it is important to maintain NPIs to prevent an uncontrolled surge in the number of infections, hospitalizations and deaths, because vaccination alone will be insufficient to control the epidemic. In parallel, accelerating the vaccination campaign, as was