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Commentary

COVID-19 vaccination and critical care capacity: Perilous months ahead

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1. Commentary

Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2), the etiologic agent of pandemic COVID-19, spread to virtually all countries around the world in the first half of 2020 [1]. It caused resurging waves of infections in the fall and winter of 2020–2021, especially in northern hemisphere countries. In many countries, hospitals experienced unsustainable pressure on their critical care capacity, as had been experienced at the pandemic onset. This has necessitated the reinstatement of national or territorial lockdowns to drastically curb the flow of inpatients. However, lockdowns have a profound negative socio-economic impact, in particular on the disadvantaged [2]. Although lockdowns are a critical and largely indispensable tool to thwart community transmission and regain control over viral pandemic spread, their repeated widespread implementation and relaxation can be particularly damaging to society. COVID-19 vaccination programs have been initiated by the end of 2020 or beginning of 2021 in a number of a countries, but the risk of renewed widespread lockdowns remains. Using available data on daily COVID-19 incidence and growth rate in eleven European countries that reinstated a national lockdown in fall 2020, we show a high risk of short-term overwhelming of critical care capacity, as levels of population immunity remain below targeted herd immunity. To avoid the repeated widespread implementation and relaxation of lock-

downs, we advocate that controlled conditions brought by current national lockdowns should be leveraged to eliminate SARS-CoV-2 circulation in the community.

Early mathematical models rapidly demonstrated the need for swift suppression of viral spread to curtail the burden on hospital care, largely due to precipitously overtaken regular and intensive care services [3–5]. When overwhelmed, healthcare systems face unsurmountable challenges for the provision of standards of care for COVID-19 and non-COVID-19 inpatients alike. Eventually, the unavoidable need for inpatient triage can dramatically increase the mortality burden and overall emerging pandemic impact. Improved standards of care and treatment options for COVID-19 patients have contributed to decreased case fatality rates in hospitals [6]. Likewise, non-pharmaceutical interventions have contributed to reduced transmission [7], as measured by the effective reproduction number (R_{eff}), *i.e.*, the average number of new cases caused by one infected individual. However, the pandemic potential of SARS-CoV-2 has intrinsically not diminished and continues to threaten society, including through the emergence of more transmissible strains, like B.1.1.7 [8] and others, with hospitals in the front line and economies suffering dramatically. Before envisaged COVID-19 vaccination coverage achieves sufficient levels of herd immunity, critical care capacity remains at risk of becoming overwhelmed.

Considering the maximum number of daily cases of COVID-19 infections occurring during the week prior to the reinstatement of a national lockdown, as a proxy to define the incidence threshold to engage into a national lockdown, one can estimate the time needed for critical care capacity to risk becoming overwhelmed,

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as a function of a baseline daily incidence, R_{eff} and corresponding doubling time (Appendix). Such approximations are justifiable when population immunity levels remain well below targeted herd immunity, as currently observed in most countries [9,10]. While the time to the incidence threshold tends to infinity when $R_{eff} = 1.0$, it rapidly decreases with small R_{eff} increments and reaches zero when the baseline incidence equals the incidence threshold (Fig. 1a). On average, the time to the incidence threshold reached 6 months with R_{eff} values of 1.10 (1.07 – 1.13) and 3 months with R_{eff} values of 1.22 (1.15 – 1.28) for the eleven European countries studied (Fig. 1b).

In those European countries that had lifted their first lockdown in May, R_{eff} averaged 1.1 (1.05 – 1.12) from May to the end of October (Fig. A1). At $R_{eff} = 1.1$, it would take an average of 6.4 (5.2 – 7.7) months to reach the incidence thresholds from average daily incidence observed in May (Table 1). In most European countries that reimposed a lockdown in fall 2020, R_{eff} remained above 1.0 since July with an average of 1.2 (1.17 – 1.23) until the end of October. At $R_{eff} = 1.2$, it would take an average of 3.1 (2.8 – 3.5) months for these countries to reach the incidence thresholds from average daily incidence observed in July (Fig. 1c and Table 1). Both estimates fit well with the actual timing of the reinstatement of

national lockdowns in the respective countries, end of October or early November 2020.

The proposed calculations have the advantage to estimate the time to risking overwhelming critical care capacity based on R_{eff} , independently of the intrinsic transmissibility of circulating viral strains. Time-varying R_{eff} estimated over the course of an epidemic accounts for the impact of public health control measures, the build-up of immunity in the population, or both. Given k the proportion of immune individuals and g the relative reduction in transmission rates due to non-pharmaceutical interventions, R_{eff} can be calculated as $R_{eff} = (1 - k)(1 - g)R_0$ [10]. The resulting relationship between k and g to maintain R_{eff} at particular values is shown in Fig. 1d.

This has important implications. The time estimates to reach the incidence threshold apply similarly to levels of population immunity conferred by previous infection or by vaccination, in the absence of control measures, when these remain below targeted herd immunity. Assuming levels of immunity to SARS-CoV-2 from previous infection and vaccination at 30% in the population, R_{eff} would be reduced to 1.75 (based on a conservative R_0 of 2.5), risking overwhelming critical care capacity typically in less than one month, in the absence of other control measures. With 30% of the

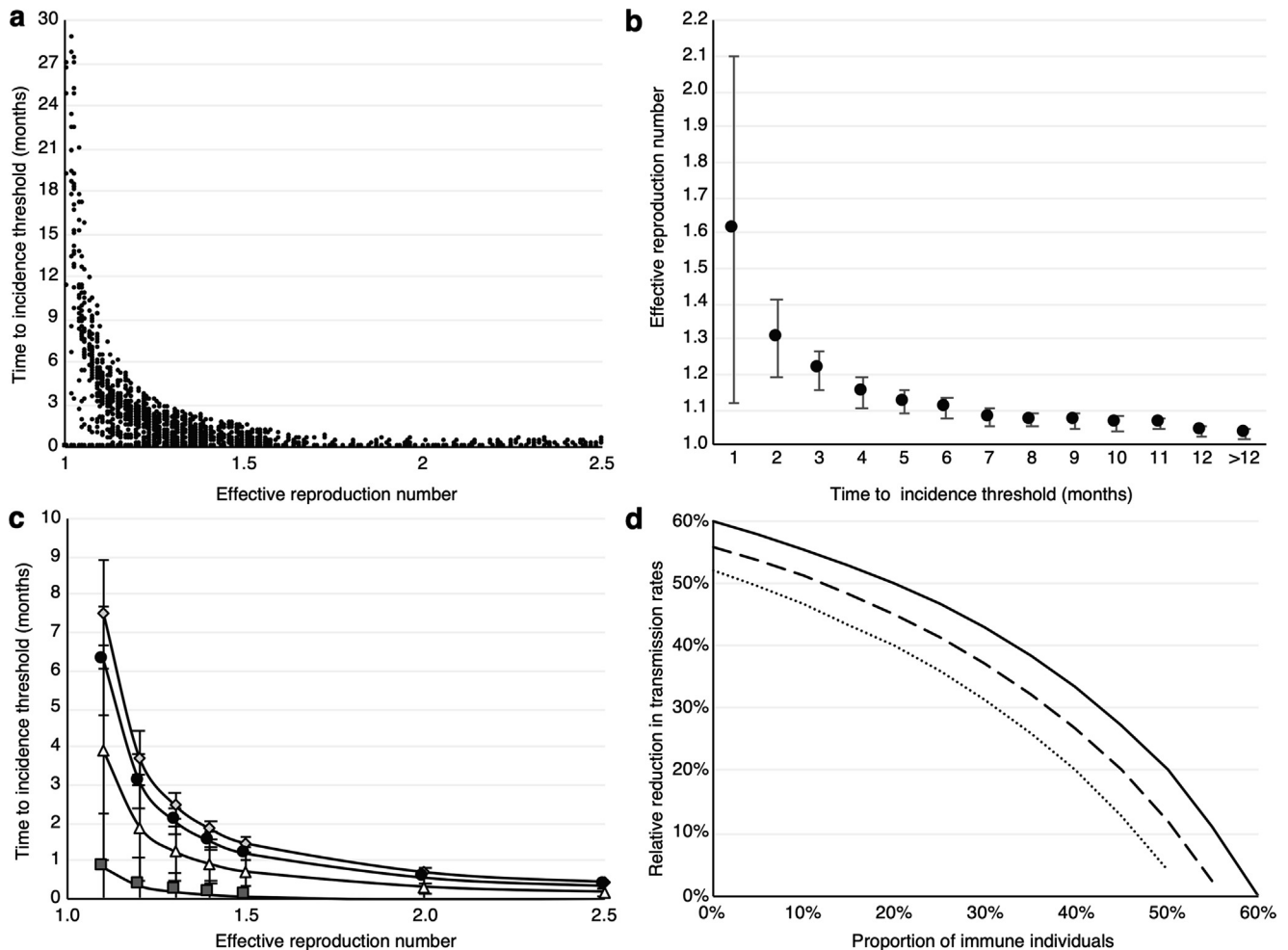


Fig. 1. Relationship between the time to reach the incidence threshold (T) and the effective reproduction number (R_{eff}) for 11 European countries reimposing a national lockdown (Austria, Belgium, Czech Republic, Germany, France, United Kingdom, Greece, Ireland, Lithuania, The Netherlands, Poland). (a) Scatterplot of calculated values of daily T as a function of daily R_{eff} over the period 1st March 2020 to 31st October 2020. (b) Average daily R_{eff} (and standard deviation) of the 11 European countries for monthly bins of daily T values. (c) Average T (and standard deviation) from baseline incidence occurring in July 2020 in the absence of vaccination (black circles) and in the presence of targeted vaccination of priority groups (grey diamonds), from baseline incidence occurring in December 2020 (dark grey squares) and from baseline incidence projected to occur upon lifting lockdowns (white triangles; see Appendix) at R_{eff} values of 1.1, 1.2, 1.3, 1.4, 1.5, 2, and 2.5. (d) Relationship between the proportion of immune individuals in the population and the relative reduction in transmission rates due to non-pharmaceutical interventions to maintain R_{eff} at 1.0 (plain line), 1.1 (dashed line) and 1.2 (dotted line). Calculations are based on a conservative R_0 of 2.5.

Table 1
Time to incidence threshold (in months) under variable conditions.

R_{eff}	From first case of COVID-19		From average baseline incidence in May		From average baseline incidence in July				From baseline incidence in December		From projected baseline incidence upon lifting lockdowns*	
	Ave	Std	Ave	Std	Without vaccination		With targeted vaccination of priority groups		Ave	Std	Ave	Std
					Ave	Std	Ave	Std				
1.01	157.3	21.8	64.6	12.5	63.1	7.1	75.2	7.1	9.3	14.0	39.4	14.0
1.05	31.4	4.4	12.9	2.5	12.6	1.4	15.0	1.4	1.8	2.8	7.8	2.8
1.1	15.6	2.2	6.4	1.3	6.2	0.7	7.5	0.7	0.8	1.4	3.9	1.4
1.2	7.8	1.1	3.2	0.6	3.1	0.4	3.7	0.4	0.4	0.7	1.9	0.7
1.3	5.1	0.7	2.1	0.4	2.0	0.2	2.4	0.2	0.2	0.5	1.2	0.5
1.4	3.8	0.5	1.6	0.3	1.5	0.2	1.8	0.2	0.1	0.4	0.9	0.4
1.5	3.1	0.4	1.2	0.3	1.2	0.1	1.4	0.1	0.1	0.3	0.7	0.3
2.0	1.5	0.2	0.6	0.1	0.6	0.1	0.7	0.1	0.0	0.1	0.3	0.1
2.5	1.0	0.1	0.4	0.1	0.4	0.05	0.4	0.05	0.0	0.1	0.2	0.1

Ave = average; Std = standard deviation.
*See Appendix for details on the calculations.

population immune, control measures would need to reduce transmission rates by 31% to maintain R_{eff} at 1.2 and by 43% to maintain R_{eff} at 1.0 (Fig. 1d). This would correspond to changes in R_{eff} (ΔR_{eff}) of -0.75 to -0.55 . The thorough analyses of Haug et al. [7] have shown that i) no single control measures have such an impact on R_{eff} and ii) that the most effective combined measures to significantly reduce R_{eff} can be particularly intrusive in restricting physical contact and movement. In other words, as population immunity levels remain low, substantial limitations on gatherings and mobility will need to be maintained upon SARS-CoV-2 circulation to prevent overwhelming of critical care capacity.

As immunity builds up in the population, the main assumption supporting the proposed approximations eventually will be falsified. However, as seen above, reaching the incidence threshold risking the overwhelming of critical care capacity inevitably calls for drastic restrictive measures, such as lockdowns, to curb the disease spread, resulting in cyclic slow-down of active virus circulation as widespread lockdowns are implemented and relaxed. This results in a stepwise population immunity build-up during each cycle. Using the same approximations as previously, the cumulative number of infections at the time of reaching the incidence threshold can be estimated based on R_{eff} (Appendix; Fig. A2). The higher R_{eff} , the shorter the time to the incidence threshold and the lower the cumulative number of infections upon reinstatement of drastic control measures. This results in a particularly slow build-up of immunity in the population, e.g. of an average of about 5% when $R_{eff} = 1.1$, and likely contributed to the seemingly low COVID-19 seroprevalence in most countries after the first wave of the pandemic [9,10]. Consequently, conditions for the proposed approximations are likely to be maintained over several successive lockdown implementation and relaxation cycles and thus several months, in the absence of vaccination and continued circulation of SARS-CoV-2.

The implementation of safe and effective vaccination programs is fraught with uncertainty and challenges, especially amidst the current climate of public hesitancy, misinformation and distrust towards vaccines [11]. Although analyses of recently developed COVID-19 vaccines suggest overall high efficacy, for example shortly after booster vaccinations [12,13], the level of efficacy and duration of protection in different age and risk groups and against transmission, including upon infection with newly emerging strains, remain to be determined. Duration of protection may be uncertain for months or years [11]. In addition, extensive research will be needed to address the differential risk factors contributing to infection, morbidity and mortality, the infectious role of younger age-groups and of individuals with asymptomatic or mild infection, the impact of ‘super-spreaders’ and individuals with

prior exposure to the virus on the spread of SARS-CoV-2 and its emerging variants, as well as the effect of vaccination on these issues. In parallel, improved surveillance at the human-animal interface will be key to inform about the risk posed by putative animal reservoirs of SARS-CoV-2, such as wildlife and farmed mink. Vaccination programs with currently licensed COVID-19 vaccines further face both logistics and strategic challenges to optimize their impact on controlling the pandemic, requiring complex calculations and well-defined sets of assumptions [11]. By the end of February 2021, COVID-19 vaccination coverage had attained levels below 20% in most countries and below 10% in many countries, including across Europe, and therefore may yet only demonstrate a modest impact on virus circulation.

Targeted vaccination of groups at risk of developing severe disease typically has been envisaged first by most governments, as these individuals make the majority of COVID-19 patients requiring intensive care. Targeted vaccination of healthcare and other essential workers is typically also a priority. Based on available data for the French population (Appendix), populations at risk and essential workers, who would receive vaccination first, may represent about 40% of the population. A vaccination coverage of 90% in these priority groups would remain below targeted herd immunity levels, even with current levels of population immunity. Reduction of virus spread by the vaccinated at-risk population may furthermore be expected to be less than that achieved by vaccinating a younger and otherwise healthy part of the population. Yet, since the vaccinated at-risk population would be protected against severe disease upon high vaccine efficacy, such approach may nonetheless reduce the risk of overwhelming critical care capacity.

Using the proposed calculations, we found that targeted vaccination programs of at-risk groups and essential workers, assuming 90% vaccination coverage and 90% effectiveness of COVID-19 vaccines against severe disease in these priority groups (Appendix), resulted in only a 1.2-month delay in reaching the incidence threshold when $R_{eff} = 1.1$ and a 0.6-month delay when $R_{eff} = 1.2$, starting from July 2020 baseline incidence (Fig. 1c and Table 1). Here also, at the time of reaching the incidence thresholds, the cumulative number of infections and vaccinated individuals remained below the population immunity levels necessary to bring R_{eff} at these respective values (Fig. A3).

It is important to note that the time to reach the incidence threshold strongly depends on the baseline incidence. In July 2020, most European countries had relatively low daily incidence of COVID-19. Higher baseline incidence may occur upon lifting ongoing lockdowns (Appendix). This would result in shorter times to reach the incidence threshold at corresponding R_{eff} , as illustrated in Fig. 1c (and Table 1). The initial deployment of vaccina-

tion against COVID-19 therefore may not prevent the overwhelming of critical care capacity in the coming months, if R_{eff} remains close to, yet above, the critical value of 1.0 upon lifting restriction measures.

The proposed calculations are based on simplified assumptions of the transmission dynamics of SARS-CoV-2 and have limitations. As seen above, the approximations can only be justified when levels of immunity in the population remain below targeted herd immunity and thus cannot apply when the build-up of immunity through infection or vaccination approaches or reaches such levels. We nonetheless argue that the proposed calculations serve their purpose to demonstrate the risk of overwhelming critical care capacity in the coming months while vaccination programs become initiated, in view of enduring uncertainties on achievable vaccination coverage and timelines. The calculations are dependent on relatively uncertain measures of daily incidence and time-varying effective reproduction numbers, based on incomplete data of varying accuracy. However, sensitivity analyses demonstrate the robustness of the calculations to variations in the estimated parameters (Table A1 and Fig. A4). The proposed calculations further assume that critical care capacity and the proportion of hospitalized patients needing intensive care remain unchanged. Critical care capacity has increased in most countries since the start of the pandemic and improved treatment options may reduce the proportion of inpatients requiring intensive care in the near future. The impact of such changes is nevertheless expected to be limited due to the different orders of magnitude between these changes and the flow of inpatients during current and potential upcoming waves.

National lockdowns are the only option left to prevent overwhelming healthcare systems in countries where the spread of COVID-19 tends to fall out of control. The WHO urges governments to avoid the use of national or widespread lockdowns as the main control strategy against COVID-19, due to the disruptive socio-economic consequences of their repeated implementation and relaxation [2]. Current mitigation strategies—aimed at controlling but not eliminating SARS-CoV-2 circulation—as adopted by most northern hemisphere countries have shown limitations in maintaining R_{eff} close to 1.0. Based on the work of Haug et al. [7], similarly restrictive measures on contact and mobility as applied during lockdowns may be necessary to maintain SARS-CoV-2 R_{eff} at sufficiently low levels to prevent repeated short-term overwhelming of critical care capacity. Continuing rigorous non-pharmaceutical interventions will be necessary before vaccination programs for the population at large achieve sufficient levels of herd immunity.

Enforcing restrictive measures over a long period tend to lead to public fatigue and waning public compliance, further complicating effective control of virus circulation levels. Mitigation strategies thus will likely be ineffective as well as unsustainable and socio-economically costly to prevent the repeated overwhelming of critical care capacity in the months to come. This calls for the implementation of control measures aiming at bringing and maintaining R_{eff} below 1.0 towards the elimination of SARS-CoV-2 community transmission, followed by prevention of COVID-19 importation and prompt stamping out of emerging clusters of infection. Such an approach has been applied successfully in coun-

tries of the eastern and south-eastern hemisphere. These countries offer relevant blueprints for the implementation of this strategy in the northern hemisphere, towards a collaborative and coordinated approach to tackle this unprecedented crisis (Appendix). Priority vaccination of frontline workers and eventually vaccination of the population at large will further strengthen the countries' purposeful response towards maintaining zero COVID-19 community transmission.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.vaccine.2021.03.035>.

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