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► To cite this version:

Davide Faranda, Tommaso Alberti, Maxence Arutkin, Valerio Lembo, Valerio Lucarini. Interrupting vaccination policies can greatly spread SARS-CoV-2 and enhance mortality from COVID-19 disease: the AstraZeneca case for France and Italy. *Chaos: An Interdisciplinary Journal of Nonlinear Science*, 2021, 31 (4), pp.041105. 10.1063/5.0050887. hal-03172578v2

HAL Id: hal-03172578

<https://hal.science/hal-03172578v2>

Submitted on 6 May 2021

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1 **Interrupting vaccination policies can greatly spread SARS-CoV-2**
2 **and enhance mortality from COVID-19 disease: the AstraZeneca**
3 **case for France and Italy**

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26 (Dated: April 12, 2021)

Abstract

Several European countries have suspended the inoculation of the AstraZeneca vaccine out of suspicion of causing deep vein thrombosis. In this letter we report some Fermi estimates performed using a stochastic model aimed at making a risk-benefit analysis of the interruption of the delivery of the AstraZeneca vaccine in France and Italy. Our results clearly show that excess deaths due to the interruption of the vaccination campaign injections largely overrun those due to thrombosis even in worst case scenarios of frequency and gravity of the vaccine side effects.

We analyze, in the framework of epidemiological modelling, the stop in the deployment of the AstraZeneca vaccine due to some suspected side effects. Indeed, few dozen suspicious cases of Deep Vein Thrombosis (DVT) over 5 millions vaccinations have arisen in Europe and pushed several European countries to suspend AstraZeneca injection. Using both an epidemiological Susceptible-Exposed-Infected-Recovered (SEIR) model and statistical analysis of publicly available data, we estimate the excess deaths resulting from missing inoculations of the vaccine and those potentially linked to DVT side effects in France and Italy. We find that, despite the many simplifications and limitations in our analysis, the excess deaths differ by at least an order of magnitude in the two strategies, that the relative benefits are wider in situations where the reproduction number is larger, and they increase with the temporal duration of the vaccine ban.

I. INTRODUCTION

As of March 2021, the spread of the SARS-CoV-2 virus [1] has caused more than 120 millions infections worldwide with a total death toll of more than 2 millions. Up to the end of 2020, the only effective measures to contain the spread of the virus were based on social distancing, wearing face masks and more/less stringent lockdown [2–4]. Later on, a

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53 massive vaccination campaign kicked off in several countries thanks to the availability of a
54 variety of vaccines (e.g., AstraZeneca, Johnson&Johnson, Moderna, Pfizer/BionTech, Sput-
55 nik V, among others). Such vaccines differ substantially in terms of efficacy, legal status,
56 availability, and logistics needed for their delivery to patients. According to various esti-
57 mates [5], vaccinations would produce a substantial reduction in infections, and eventually
58 yield to "herd immunity" when $\approx 70\%$ of the population gets fully vaccinated. When such
59 a large fraction of the population becomes immune to the disease, its spread from person
60 to person becomes very unlikely, and the whole community becomes protected. By allowing
61 for an earlier easing of non-medical measures against the SARS-CoV-2 virus, vaccination
62 is also expected to significantly reduce the economical, social and psychological impacts of
63 lockdown measures [6]. Those estimates assume that there is no break in the supply of
64 vaccines or any other suspension in the procedure due to side effects from vaccination. On
65 March 15th 2021 several European countries suspended the use of AstraZeneca COVID-19
66 vaccine as a precaution in order to investigate the death of a few dozens of patients devel-
67 oping blood clots - associated with Deep Vein Thrombosis (DVT) [7] - after such vaccine.
68 Health personnel who inoculated the vaccine to those who died as a result of DVT are being
69 investigated in Italy for manslaughter [8]. The contingent situation with the widespread
70 COVID-19 pandemic naturally raises the question of whether a prolonged stop in vaccina-
71 tions coming from adopting the precautionary principle [9] could cause an excess mortality
72 beyond that caused by hypothetical side effects of the vaccines. The European Medicines
73 Agency (EMA) is currently assessing whether the vaccine can continue to be used despite
74 possibly causing this very rare side effect. In this work, we aim at exploring this issue by
75 computing future COVID-19 epidemic scenarios by comparing i) the excess mortality caused
76 by reducing the vaccinations using the stochastic Susceptible-Exposed-Infected-Recovered
77 (SEIR) model [10], and ii) the estimates of the possible casualties caused by side effects of
78 a vaccine, namely those associated with DVT. We remark that the additional, longer-term
79 effect of the presence of higher infection rates, e.g. the increased risk of virus mutations
80 leading to possibly more malignant and/or more infectious variants, is not included in our
81 treatment. Our analysis focuses on France and Italy, which have been among the countries
82 that have been most severely impacted by the COVID-19 pandemic [11]. An important
83 remark follows. Our goal is not to provide an exact estimate of both i) and ii) but rather
84 to perform an order-of-magnitude comparison between excess deaths resulting from differ-

85 ent scenarios of vaccination policy. We proceed in the spirit of complexity science, where
86 simple models are useful for elucidating the main mechanisms behind complex behaviour
87 and provide useful inputs for the deployment of more advanced modelling suites and data
88 collection strategies [12–16]. In other words, we will approach the problem by performing
89 Fermi estimates [17] where the classical back-of-the-envelope calculations are performed via
90 the SEIR model, allowing to take into account the uncertainties in both model parameters
91 and data. *In nuce*, we perform a counterfactual analysis based on a story-line approach,
92 which has become a powerful investigation method for assessing risks coming from extreme
93 events [18]. While the quantitative consolidation of our results clearly requires extensive
94 data analysis and modelling, our findings show with a large confidence that excess deaths
95 due to the interruption of the vaccination campaign largely override those due to DVT
96 even in the worst case scenarios of frequency and gravity of the vaccine side effects. Fermi
97 estimates can provide valuable inputs for an efficient and pragmatic application of the pre-
98 cautionary principle able to reduce the negative impacts of hazards of various nature, as
99 done in economics [19].

100 II. METHODS

101 The model [20] with time-dependent control parameters can mimic the dependence on
102 additional/external factors such as variability in the detected cases, different physiological
103 response to the virus, release or reinforcement of distancing measures [10]. Our compart-
104 mental model [21] divides the population into four groups, namely Susceptible (S), Exposed
105 (E), Infected (I), and Recovered (R) individuals, according to the following discrete-time
106 evolution equations:

$$S_{t+1} = -\lambda(1-\alpha)\frac{I_t S_t}{N_t} - \lambda\alpha(1-\sigma)\frac{I_t S_t}{N_t} + (1-\sigma\alpha)S_t \quad (1)$$

$$E_{t+1} = \lambda(1-\alpha)\frac{I_t S_t}{N_t} + \lambda\alpha(1-\sigma)\frac{I_t S_t}{N_t} + (1-\epsilon)E_t \quad (2)$$

$$I_{t+1} = \epsilon E_t + (1-\alpha-\beta)I_t \quad (3)$$

$$R_{t+1} = R_t + \sigma\alpha S_t + \beta I_t \quad (4)$$

107 In the SEIR model above, the classical parameters are the recovery rate (β), the inverse
 108 of the incubation period (ϵ), and the infection rate (λ). Here we have generalized the model
 109 presented in Faranda and Alberti [10] by introducing two additional parameters able to
 110 succinctly mimic the strategies of a vaccination campaign, namely the vaccination rate per
 111 capita α and the vaccine efficacy σ , see Sun and Hsieh [22]. In order to consider uncertainties
 112 in long-term extrapolations and time-dependent control parameters, a stochastic approach is
 113 used through which the control parameters $\kappa \in \{\alpha, \beta, \epsilon, \lambda, \sigma\}$ are described by an Ornstein-
 114 Uhlenbeck process [23] with drift as follows:

$$115 \quad d\kappa = -\kappa(t)dt + \kappa_0 dt + \varsigma_\kappa dW_t, \quad (5)$$

116 where $\kappa_0 \in \{\alpha_0, \beta_0, \epsilon_0, \lambda_0, \sigma_0\}$, dW_t is the increment of a Wiener process. We remind that
 117 the basic reproduction number [24] is written as $R_0 = \beta_0/\lambda_0$. In Eqs. (1)-(5) we set $dt = 1$,
 118 which is the highest time resolution available for official COVID-19-related counts and is
 119 relatively small compared to the characteristic times associated with COVID-19 infection,
 120 incubation, and recovery/death.

α_0	β_0	ϵ_0	σ_0	m_0
0.0015 [see Ref. 25]	0.37 [see Ref. 10]	0.27 [see Ref. 26]	0.59 [see Ref. 27]	0.015 [see Ref. 28]
ς_α	ς_β	ς_ϵ	ς_σ	ς_m
0.25 [see Ref. 25]	0.2 [see Ref. 20]	0.2 [see Ref. 25]	0.1 [see Ref. 27]	0.0

TABLE I. Model parameters used for our simulations with corresponding references.

121 Initialising parameters with their associated reference are shown in Table I. The mortality
 122 rate m_0 is also shown, set to 0.015 [28]. While β_0 and ϵ_0 and the associated ς are the same as

123 in [10], the values of σ_0 and respective ς are derived from the range given for the AstraZeneca
 124 vaccine phase 3 tests for the first dose [27], and α_0 and ς_α are given supposing that both
 125 Italy and France keep vaccinating 10^5 individuals per day with a 20% daily fluctuation [25].
 126 As in [10], we also set $\varsigma_\lambda = 0.2$, allowing for 20% daily fluctuations in the infection rate.
 127 Note that here we restrict to Gaussian fluctuations: as shown in [10], allowing for log-normal
 128 fluctuations of the parameters does not change the average results but slightly enhance their
 129 dispersion. See Supplementary Material for the numerical code.

130 **III. ESTIMATE OF THE EXCESS DEATHS DUE TO STOPPING ASTRAZENECA** 131 **VACCINE INOCULATION**

132 Figure 1 reports the daily number of deaths $m_0 \times I_t$ as a function of time for Italy (a) and
 133 France (b). Initial conditions are set for both countries to the values reported on March 15th
 134 as follows: for Italy, we set $N = 60 \cdot 10^6$ population, $E_{t=1} = I_{t=1} = 20 \cdot 10^4$ as the infected
 135 and exposed populations, $R_{t=1} = 11 \cdot 10^6$ as the sum of $9 \cdot 10^6$ recovered estimated from
 136 serologic tests and $2 \cdot 10^6$ immunized from 2 doses of either Pfizer/BioNTech, Moderna or
 137 AstraZeneca vaccines and $R_0 = 1.16$. For France, we set $N = 67 \cdot 10^6$, $E_{t=1} = I_{t=1} = 25 \cdot 10^4$,
 138 $R_{t=1} = 13.2 \cdot 10^6$ as the sum of $11 \cdot 10^6$ recovered estimated from serologic tests and $2.2 \cdot 10^6$
 139 immunized from vaccines and $R_0 = 1.02$. For both France and Italy, we assume that the
 140 virus, after the second wave, has infected the 15% of the population. This estimates are
 141 based on Pullano *et al.* [29] who reported a $7\% \pm 3\%$ total infections for France after the
 142 first wave, assuming that the second wave had a similar magnitude for both countries. We
 143 remark however, that our results are basically insensitive to oscillation of $S(1)$ of order of
 144 5 millions individuals (cfr. Supplementary Material Figure S1). Rather than integrating
 145 the Fokker-Planck equation [30] corresponding to the system of equations given above, we
 146 follow a Monte Carlo approach and we perform two sets of $N_r = 1000$ realizations (see
 147 supplementary material Figure S2 for a justification of this value): stopping (red) and
 148 continuing (blue) the vaccination campaign at the same rate. The model is integrated for
 149 500 days, that is about the time it would take to vaccinate the rest of the susceptible population
 150 with AstraZeneca at the rate of 10^5 individuals per day.

152 First, we observe a monotonic decrease in the daily deaths for all scenarios considered
 153 from the initial date $t = t_0$ corresponding to March 15, 2021. This is in agreement with early

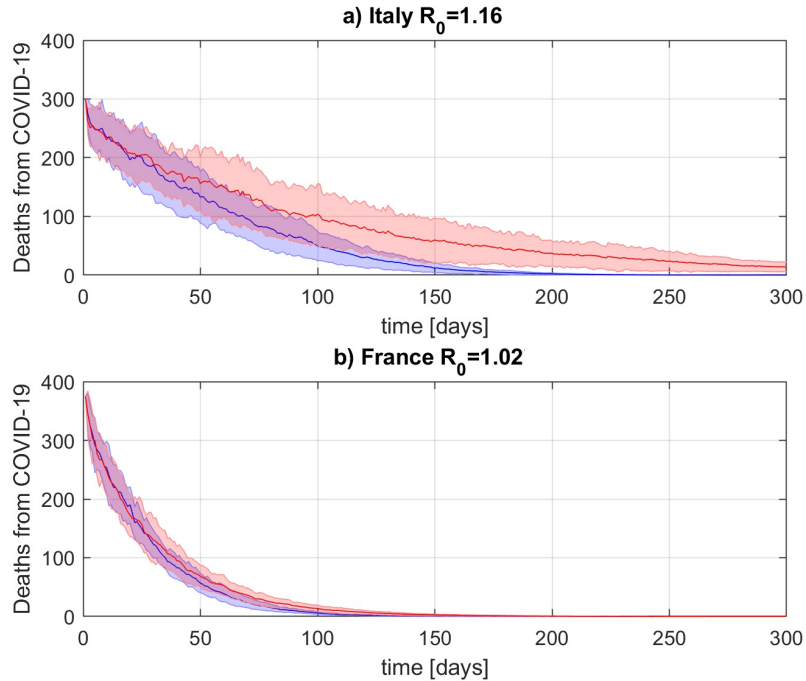


FIG. 1. The number of daily deaths $m \times I(t)$ as a function of time (300 out of 500 days shown) for Italy (a) and France (b) using the values of $R_0 = 1.16$ (Italy) and $R_0 = 1.02$ reported respectively for the 15th of March in the two analysed countries. Solid lines show the ensemble average, colored bars extend to one standard deviation of the mean. Red and blue curves refer respectively to no vaccination and a vaccination campaign whose efficacy is 59%.

154 March estimates that for Italy and France the so-called third wave should reach its peak
 155 in the second half of March, 2021 [31] Moreover, we observe that the cumulative number
 156 of deaths significantly (we take the width of the error bars as level of significance) reduces
 157 if vaccinations are continued at 100000 doses per day with respect to the scenario where
 158 vaccination is stopped. For Italy (France) completely halting the vaccination, at the actual
 159 epidemic rate, the number of excess deaths from COVID19 would amount to $9 \pm 3 \cdot 10^3$
 160 ($1.2 \pm 0.4 \cdot 10^3$) excess deaths from COVID19. The difference between the two countries
 161 is largely due to the value of R_0 , which is larger for Italy. This suggests that halting
 162 vaccination in a growing epidemics phase (Italy) has more dramatic consequences than in a
 163 more controlled scenario of $R_0 \approx 1$ (France).

164 Our previous analysis is based on a total stop of AstraZeneca vaccination. However,
 165 a more realistic scenario is to assume that AstraZeneca vaccination will resume after a

166 limited number of days used for verification. We investigate this effect in Fig. 2. There,
167 we consider the average excess deaths as a function of the interruption length in number of
168 days (x-axis) and R_0 (y-axis) for Italy (a) and France (b). The excess deaths are computed
169 with respect to a base scenario where vaccine injections are never interrupted and they
170 are averaged over 1000 realizations of the SEIR model. Figure 2 shows that the longer is
171 the vaccine injections disruption, the higher is the number of excess deaths. The impact
172 is stronger for higher values of R_0 . While waiting the advice of EMA about AstraZeneca
173 safety, many national health agencies also announced that, when allowed, they would resume
174 the vaccination at a higher rate than before to override the effects of the stop. In the
175 supplementary Figure S3 we therefore present a set of simulation where, for a number of
176 days equal to those of the vaccination interruption, injections are performed at a double
177 rate than originally planned, i.e., $2 \cdot 10^5$ individuals/day, in order to compensate for the lost
178 vaccinations. Although reduced, the number of excess deaths is still high and of the same
179 order of magnitude as the one estimated in Fig. 2, as a result of the nonlinear cascade effect
180 of the extra infections occurred in the period when vaccinations were interrupted. A focus
181 on the actual values of R_0 for Italy and France is reported in Fig. 3. Here we compare the
182 two countries and we also show the effect of doubling vaccination rates. This shows that
183 excess deaths scale down by a factor two but they remain of the same order of magnitude
184 as for the case of a business-as-usual vaccination rate, namely 10^5 vaccinations/day.

185 IV. WORST CASE SCENARIOS FOR ASTRAZENECA SIDE EFFECTS

186 The final step in our investigation is to compare the previous estimates of excess deaths
187 with an order of magnitude estimate of deaths due to DVT resulting from side effects
188 of the AstraZeneca vaccine. In order to make a meaningful comparison, in a case where
189 uncertainties are very large and hard to quantify, we will consider a worst case scenario for
190 the impacts of the side effects. This scenario relies on the unrealistic hypothesis that the
191 totality of susceptible population to DVT suffers from DVT shortly after being vaccinated,
192 and the lethality rate is similar to the one observed in the overall population.

193 As of March 15th 2021, few dozens suspect cases of DVT have been reported over a
194 number of 5 millions vaccinated people with AstraZeneca in Europe[32]. By suspect cases
195 we mean people who have developed DVT in the few days following the vaccination. This

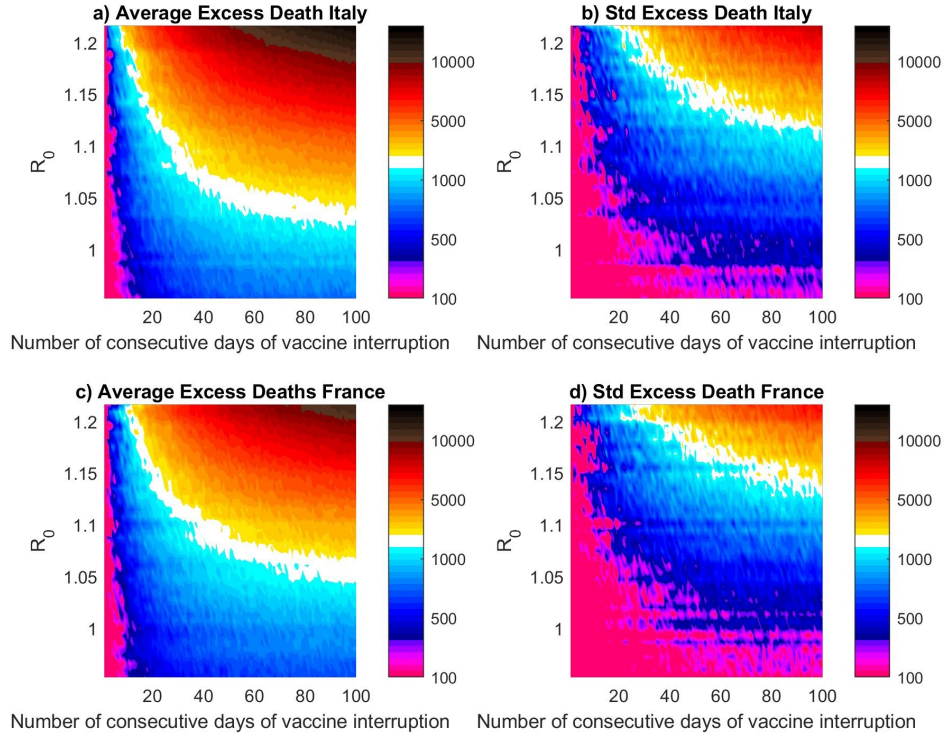


FIG. 2. (a,c) Average and (b,d) standard deviation over $N_r = 1000$ realizations of the stochastic SEIR model showing the excess deaths $m \times I(t)$ as a function of the number of the days of interruption of AstraZeneca vaccinations (x-axis) and R_0 (y-axis) for Italy (a,b) and France (c,d). The excess deaths are computed with respect to a base scenario where vaccine injections are never interrupted. Note that x-axis starts at $N = 1$. Each realization of the SEIR model is integrated for 500 days.

196 leads us to an estimate of a frequency of 6 cases per million of vaccines. Let us call this
 197 rate r_{AZ}^{DVT} . Let us also consider that, in the case of France, the incidence of DVT has been
 198 estimated to 1800 people per 1 million inhabitants per year ([33]), with a lethality rate after
 199 three months of 5% [34], raising to 30% when a period of 5 years is considered [7]. This
 200 leads to estimating a total of the order of 10000 deaths per year as a result of DVT. Even
 201 assuming that all DVT cases following the inoculation of the AstraZeneca vaccine would
 202 have not manifested themselves in absence of the injection, we have that N vaccinations
 203 would lead to an extra $N \times r_{AZ}^{DVT}$ DVT cases. Let us assume that all of these cases result
 204 into death[35]. We then have that 10^5 daily vaccinations would result into a maximum of
 205 0.6 daily deaths. In 500 days, which is the time needed to cover the entirety of the French

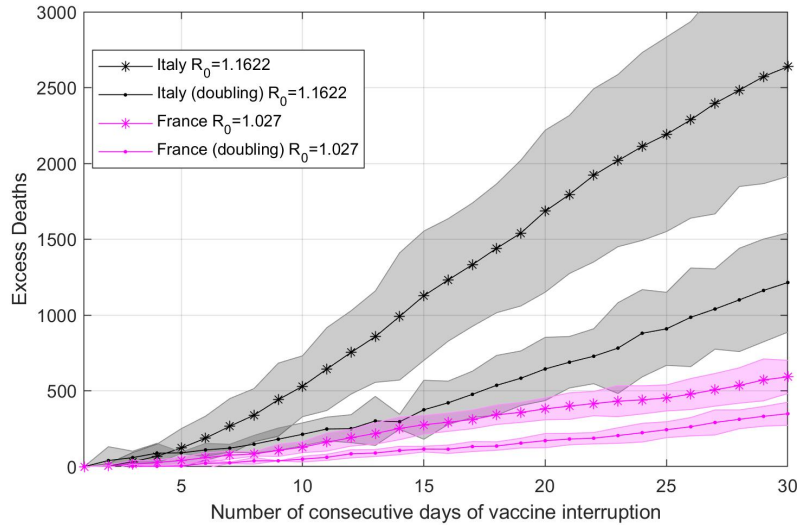


FIG. 3. Average over $N_r = 1000$ realizations of the stochastic SEIR model showing the excess deaths $m \times I(t)$ as a function of the number of the days of interruption of AstraZeneca vaccinations for Italy $R_0 = 1.16$ (black and France $R_0 = 1.02$ (magenta)). Simulations are smoothed with a moving average filter with window size 10 days. Stars indicate simulations where vaccinations are resumed at the same rate, dots indicate simulations where the vaccination rate is doubled for a number of days equivalent to those of interruption. Error bars are computed as the mean relative error.

206 population, this leads to an upper bound of 300 deaths. Considering a death rate of 30%,
 207 the number scales down to approximately 100, while considering a death rate of 5% the
 208 number scales down to approximately 15. Similar figures apply for Italy.

209 V. CONCLUSION

210 Decision-making in presence of strong uncertainties associated with health and environ-
 211 mental risks is an extremely complex process, resulting from the interplay between science,
 212 politics, stakeholders, activists, lobbies, media, and society at large [36–38]. In this letter,
 213 we have aimed at contributing to the debate on different strategies for combating, in condi-
 214 tions of great uncertainties in terms of health and social response, pandemic like the current
 215 one caused by the SARS-CoV-2 virus. We have focused on the case of the AstraZeneca
 216 COVID-19 vaccine and on the locales of Italy and France, for the period starting on March

217 15th 2021. The goal is providing a semi-quantitative comparison, based on Fermi estimates
218 informed by a simple yet robust stochastic model, between the excess deaths due to tempo-
219 ral restriction in the deployment of a still experimental vaccine and the excess deaths due
220 to its possible side effects. Given the many uncertainties on the (possible) side effects of
221 the vaccine, we have resorted to making worst case scenario calculations in order to pro-
222 vide a robust upper bound to the related excess deaths. Our results are preliminary and
223 should be supplemented by more detailed modelling and data collection exercises. Indeed:
224 i) we assume a single vaccine with the nominal AstraZeneca efficacy, neglecting the other
225 available vaccines, ii) we consider a fixed vaccination rate, iii) for AstraZeneca DVT side
226 effects we consider French data and rescale them for the Italian populations, iv) we focused
227 our analysis on DVT side effects, but other pathologies could be considered with the same
228 approach. Yet, these results clearly suggest - see a useful summary in Table II - that the
229 benefits of deploying the vaccine greatly outweigh the associated risks, and that the relative
230 benefits are wider in situations where the reproduction number is larger, and they increase
231 with the temporal duration of the vaccine ban. We have also analysed the case of resuming
232 the vaccinations at a double rate ($2 \cdot 10^5$ vaccinations/day) for an amount of days equal
233 to vaccine interruption period (Fig. 3 and Fig. S3). This analysis has pointed out that
234 excess deaths are still of the same order of magnitude as those observed by resuming vac-
235 cinations with 10^5 vaccinations/day injection rate but scale down by a factor 2. This is a clear
236 outcome of the nonlinear effects of epidemiological dynamics: those who have not been vac-
237 cinated can contaminate other individuals before vaccination resume, as a result of a cascade
238 mechanism also observed in turbulent flows: there, energy injected in large scales vortex is
239 transferred to small scales via nonlinear interactions between scales [39]. Here, in analogy,
240 a few non-vaccinated individuals can produce a large number of infected individuals. The
241 process can only stop if a huge number of daily vaccinations (much larger than a factor
242 2) is performed. Nevertheless, this still requires a characteristic recovery timescale T that
243 is larger than the typical immunization scale η (e.g., a few months for AstraZeneca [27]).
244 Finally, even if several countries have resumed, or are going to resume, AstraZeneca vaccina-
245 tions, the effect of the interruption is hard to counterbalance and require vaccination efforts
246 difficult to set-up in due times. Furthermore, at least for large countries where AstraZeneca
247 vaccination could resume, the confidence of the population in the vaccines is reduced by a
248 non negligible percentage [40]. In this sense, our estimates are likely to be conservative and

Excess Deaths	Italy	France
Stop AZ for $t = 500$ days	9000 ± 3000	1200 ± 400
Stop AZ for $t = 14$ days	1700 ± 500	430 ± 70
Stop AZ for $t = 7$ days	790 ± 90	160 ± 30
Stop AZ for $t = 3$ days	260 ± 50	130 ± 20
Worst case DVT deaths due to AZ	≈ 280	≈ 300
High fatality DVT deaths due to AZ	≈ 90	≈ 100
Standard fatality DVT deaths due to AZ	≈ 13	≈ 15

TABLE II. The first 4 lines of the table indicate the excess deaths due to the interruption of AstraZeneca compared to a reference scenario where the vaccine injections are never interrupted. The SEIR model is integrated for 500 days with $R_0 = 1.16$ for Italy and $R_0 = 1.02$ for France. The last 3 rows of the table show the deaths from deep vein thrombosis (DVT) that could be due to the vaccine in three different scenarios: the worst case (100% mortality rate), a high mortality scenario (death rate of 30%) and a standard mortality scenario (5% mortality rate) assuming a period of 500 days.

249 might possibly underestimate the excess deaths deriving from the disbelief in the vaccina-
250 tion policies observed in the largest European countries. The analysis presented here has
251 been performed with a parsimonious but well-posed and tested model and we hope that the
252 results we obtain might be the starting point for more detailed, more advanced, and more
253 mature investigations with sophisticated models and data collection exercises.

254 SUPPLEMENTARY MATERIAL

255 The supplementary Material available at [link will be inserted after publication] contains
256 the numerical code used in this study and three supplementary figures.

257 ACKNOWLEDGEMENTS

258 This work has been greatly supported by the London Mathematical Laboratory and we
259 acknowledge the logistic support of SCuP. VLu acknowledges the support received from the
260 EPSRC project EP/T018178/1 and from the EU Horizon 2020 project TiPES (Grant no.

261 820970). This is TiPES' contribution #97. We thank A Veber, A Mazaud, FM Breon,
262 the Modcov19 CNRS community and two anonymous reviewers for useful comments and
263 suggestions.

264 DATA AVAILABILITY

265 Raw data that support the findings of this study are openly available in Johns Hop-
266 kins University Center for Systems Science at [https://systems.jhu.edu/research/
267 public-health/ncov/](https://systems.jhu.edu/research/public-health/ncov/). Derived data supporting the findings of this study are available
268 from the corresponding author upon reasonable request.

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- 269 [1] J. Wu, W. Cai, D. Watkins, and J. Glanz, How the virus got out, The New York Times
270 (2020).
- 271 [2] R. M. Anderson, H. Heesterbeek, D. Klinkenberg, and T. D. Hollingsworth, How will country-
272 based mitigation measures influence the course of the covid-19 epidemic?, The Lancet **395**,
273 931 (2020).
- 274 [3] M. Chinazzi, J. T. Davis, M. Ajelli, C. Gioannini, M. Litvinova, S. Merler, A. Pa-
275 store y Piontti, K. Mu, L. Rossi, K. Sun, C. Viboud, X. Xiong, H. Yu, M. E.
276 Halloran, I. M. Longini, and A. Vespignani, The effect of travel restrictions on the
277 spread of the 2019 novel coronavirus (covid-19) outbreak, Science **368**, 395 (2020),
278 <https://science.sciencemag.org/content/368/6489/395.full.pdf>.
- 279 [4] H.-Y. Yuan, G. Han, H. Yuan, S. Pfeiffer, A. Mao, L. Wu, and D. Pfeiffer, The importance
280 of the timing of quarantine measures before symptom onset to prevent covid-19 outbreaks -
281 illustrated by hong kong's intervention model, medRxiv 10.1101/2020.05.03.20089482 (2020),
282 <https://www.medrxiv.org/content/early/2020/05/06/2020.05.03.20089482.full.pdf>.
- 283 [5] D. Sridhar and D. Gurdasani, Herd immunity by infection is not an option, Science **371**, 230
284 (2021), <https://science.sciencemag.org/content/371/6526/230.full.pdf>.
- 285 [6] N. Fernandes, Economic effects of coronavirus outbreak (covid-19) on the world economy,
286 Available at SSRN 3557504 (2020).

- 287 [7] M. Cushman, Epidemiology and risk factors for venous thrombosis, *Seminars in hematology*
288 **44**, 62 (2007).
- 289 [8] ANSA, March 2021: <https://tinyurl.com/4ywxt5kp>.
- 290 [9] K. Steele, The precautionary principle: a new approach to public decision-
291 making?, *Law, Probability and Risk* **5**, 19 (2006), [https://academic.oup.com/lpr/article-](https://academic.oup.com/lpr/article-pdf/5/1/19/6207484/mgl010.pdf)
292 [pdf/5/1/19/6207484/mgl010.pdf](https://academic.oup.com/lpr/article-pdf/5/1/19/6207484/mgl010.pdf).
- 293 [10] D. Faranda and T. Alberti, Modeling the second wave of COVID-19 infections in France and
294 Italy via a stochastic SEIR model, *Chaos* **30**, 111101 (2020), arXiv:2006.05081 [q-bio.PE].
- 295 [11] T. Alberti and D. Faranda, On the uncertainty of real-time predictions of epidemic growths: A
296 covid-19 case study for china and italy, *Communications in Nonlinear Science and Numerical*
297 *Simulation* **90**, 105372 (2020).
- 298 [12] I. M. Held, The gap between simulation and understanding in climate modeling, *Bulletin of*
299 *the American Meteorological Society* **86**, 1609 (2005).
- 300 [13] M. Pascual, M. Roy, and K. Laneri, Simple models for complex systems: exploiting the rela-
301 tionship between local and global densities, *Theoretical Ecology* **4**, 211 (2011).
- 302 [14] U. Gähde, S. Hartmann, and J. Wolf, *Models, Simulations, and the Reduction of Complexity*,
303 *Abhandlungen der Akademie der Wissenschaften in Hamburg* (De Gruyter, 2013).
- 304 [15] P. Almaraz, Simple models, complex models, useful models: can we tell them from the flap of
305 a butterfly’s wings?, *Frontiers in Ecology and Evolution* **2**, 54 (2014).
- 306 [16] M. Ghil and V. Lucarini, The physics of climate variability and climate change, *Rev. Mod.*
307 *Phys.* **92**, 035002 (2020).
- 308 [17] S. Mahajan, *The Art of Insight in Science and Engineering: Mastering Complexity* (The MIT
309 Press, Cambridge, USA, 2014).
- 310 [18] T. G. Shepherd, A common framework for approaches to extreme event attribution, *Current*
311 *Climate Change Reports* **2**, 28 (2016).
- 312 [19] P. M. Anderson and C. A. Sherman, Applying the fermi estimation technique to business
313 problems., *Journal of Applied Business & Economics* **10** (2010).
- 314 [20] D. Faranda, I. P. Castillo, O. Hulme, A. Jezequel, J. S. W. Lamb, Y. Sato, and E. L. Thomp-
315 son, Asymptotic estimates of sars-cov-2 infection counts and their sensitivity to stochastic
316 perturbation, *Chaos: An Interdisciplinary Journal of Nonlinear Science* **30**, 051107 (2020),
317 <https://doi.org/10.1063/5.0008834>.

- 318 [21] F. Brauer, Compartmental models in epidemiology, in *Mathematical epidemiology* (Springer,
319 2008) pp. 19–79.
- 320 [22] C. Sun and Y.-H. Hsieh, Global analysis of an seir model with varying population size and
321 vaccination, *Applied Mathematical Modelling* **34**, 2685 (2010).
- 322 [23] G. E. Uhlenbeck and L. S. Ornstein, On the theory of the brownian motion, *Phys. Rev.* **36**,
323 823 (1930).
- 324 [24] Paul L. Delamater et al., Complexity of the basic reproduction number (r_0) - volume 25,
325 number 1-january 2019 - emerging infectious diseases journal - cdc (2019).
- 326 [25] L. Salvioli, Il vaccino anti covid in italia in tempo reale: Il sole 24 ore (2021).
- 327 [26] S. A. Lauer, K. H. Grantz, Q. Bi, F. K. Jones, Q. Zheng, H. R. Meredith, A. S. Azman, N. G.
328 Reich, and J. Lessler, The incubation period of coronavirus disease 2019 (covid-19) from
329 publicly reported confirmed cases: Estimation and application, *Annals of Internal Medicine*
330 (2020).
- 331 [27] Merryn Voysey et al., Safety and efficacy of the chadox1 ncov-19 vaccine (azd1222) against
332 sars-cov-2: an interim analysis of four randomised controlled trials in brazil, south africa, and
333 the uk, *The Lancet*, *The Lancet* **397**, 99 (2021).
- 334 [28] D. Fanelli and F. Piazza, Analysis and forecast of COVID-19 spreading in China, Italy and
335 France, *Chaos Solitons and Fractals* **134**, 109761 (2020), arXiv:2003.06031 [q-bio.PE].
- 336 [29] G. Pullano, L. Di Domenico, C. E. Sabbatini, E. Valdano, C. Turbelin, M. Debin, C. Guerrisi,
337 C. Kengne-Kuetche, C. Souty, T. Hanslik, *et al.*, Underdetection of cases of covid-19 in france
338 threatens epidemic control, *Nature* **590**, 134 (2021).
- 339 [30] H. Risken, *The Fokker-Planck equation* (Springer, Berlin, 1996).
- 340 [31] The Guardian, March 2021: <https://tinyurl.com/vvwhcydz>.
- 341 [32] Here, we use European data accessible via the website of the European Medicines Agency at
342 <https://tinyurl.com/ht8y98kr> to average out the large spread of national data.
- 343 [33] S. Bouée, C. Emery, A. Samson, J. Gourmelen, C. Bailly, and F.-E. Cotté, Incidence of venous
344 thromboembolism in France: a retrospective analysis of a national insurance claims database,
345 *Thrombosis Journal* **14**, 4 (2016).
- 346 [34] J. A. Heit, Epidemiology of venous thromboembolism, *Nature Reviews Cardiology* **12**, 464
347 (2015).
- 348 [35] Current data suggest that this is manifestly a gross worst case approximation.

- 349 [36] Anonymous, Agu statement: Investigation of scientists and officials in l'aquila,
350 italy, is unfounded, *Eos, Transactions American Geophysical Union* **91**, 248 (2010),
351 <https://agupubs.onlinelibrary.wiley.com/doi/pdf/10.1029/2010EO280005>.
- 352 [37] A. Benessia and B. De Marchi, When the earth shakes . . . and science with it. the management
353 and communication of uncertainty in the l'aquila earthquake, *Futures* **91**, 35 (2017), post-
354 Normal science in practice.
- 355 [38] J. Reis and P. S. Spencer, Decision-making under uncertainty in environmental health policy:
356 new approaches, *Environmental Health and Preventive Medicine* **24**, 57 (2019).
- 357 [39] A. Kolmogorov, The Local Structure of Turbulence in Incompressible Viscous Fluid for Very
358 Large Reynolds' Numbers, *Akademiia Nauk SSSR Doklady* **30**, 301 (1941).
- 359 [40] *The Economist*, March 2021: <https://tinyurl.com/83cbr4d3>.

Supplemental Material for: Interrupting vaccination policies can greatly spread SARS-CoV-2 and enhance mortality from COVID-19 disease: the AstraZeneca case for France and Italy

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(Dated: April 3, 2021)

Abstract

The supplemental Material for "Interrupting vaccination policies can greatly spread SARS-CoV-2 and enhance mortality from COVID-19 disease: the AstraZeneca case for France and Italy" contains: i) the numerical code used in this study, ii) three supplementary figures.

I. NUMERICAL CODE

```
%Numerical SEIR code for "Interrupting vaccination policies can greatly spread
%SARS-CoV-2 and enhance mortality from COVID-19 disease: the AstraZeneca case
%for France and Italy" by Faranda et al.
%This code integrates the SEIR Model with vaccination policies interrupted for 7 days.
%The data are referred to the Italian population
```

```
Country='Italy';
```

```
%Population;
```

```
N=60000000;
```

```
%Initial conditions
```

```
S(1)=N-9000000-2000000; %Susceptibles, including those
```

```
%who had the virus in the first and second wave (9 millions)
```

```
%and those who received two doses vaccines
```

```
E(1)=20000; %Exposed
```

```
I(1)=20000; %Infected
```

```
R(1)=11000000; %Recovered
```

```
%Parameters
```

```
alpha0=100000./N ; %Vaccination rate
```

```
sigma0=0.59 ; % Vaccine Efficacy
```

```
epsilon0=0.27 ; %Incubation Rate
```

```
beta0=0.37; %Recovery Rate
```

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```

lambda0=0.45 %Infection Rate
mort0=0.015; %Mortality
R0=lambda0./beta0; %Basic Reproduction number

%Dynamical steps
t_susp=7; %example where the vaccination is suspended for one week
Tint=500;

for t=1:Tint
%F
if t<t_susp
alpha=0;
sigma=0;
epsilon=epsilon0 +0.2*epsilon0*randn;
beta=beta0+0.2*beta0*randn;
lambda=lambda0+0.2*lambda0*randn;
else
alpha=alpha0+0.25*alpha0*randn;
sigma=sigma0+0.1*sigma0*randn;
epsilon=epsilon0 +0.2*epsilon0*randn;
beta=beta0+0.2*beta0*randn;
lambda=lambda0+0.2*lambda0*randn;
end

K(t)=I(t)*S(t)./N;
S(t+1)=S(t)-lambda*(1-alpha)*K(t)-(1-sigma)*alpha*lambda*K(t)-sigma*alpha*S(t);
E(t+1)=E(t)+lambda*(1-alpha)*K(t)+(1-sigma)*alpha*lambda*K(t)-epsilon*E(t);
I(t+1)=I(t)+epsilon*E(t)-(alpha+beta)*I(t);
R(t+1)=R(t)+sigma*alpha*S(t)+beta*I(t);
M(t+1)=0.015*I(t);

end

```

II. SUPPLEMENTARY FIGURES

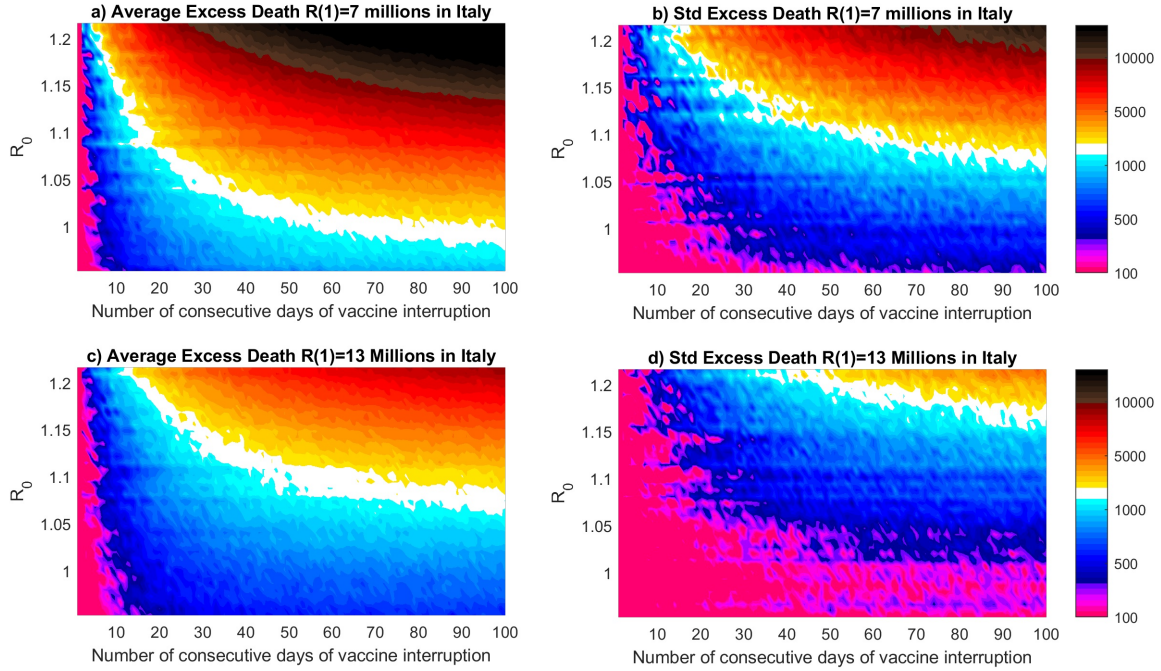


FIG. 1. (a,c) Average and (b,d) standard deviation over $N_r = 1000$ realizations of the SEIR model showing the excess deaths $m \times I(t)$ as a function of the number of the days of interruption of AstraZeneca vaccinations (x -axis) and R_0 (y -axis) for Italy with $R(1) = 7$ millions (a,b) and $R(1) = 13$ millions (c,d). The excess deaths are computed with respect to a base scenario where vaccine injections are never interrupted. Arrows indicate the values of R_0 chosen for Figs. 2 and 3. The model is integrated for 500 days. x -axis starts at $N = 1$

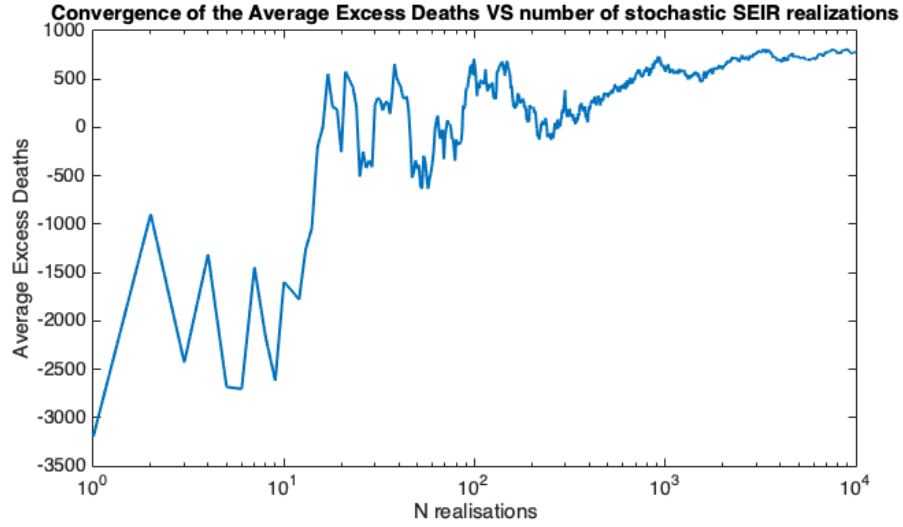


FIG. 2. Convergence in number of realisation N_r (x-axis) of the average excess deaths (y-axis) in Italy after a 5 days interruption of AstraZeneca vaccinations. The excess deaths are computed with respect to a base scenario where vaccine injections are never interrupted. The average excess deaths achieve a good convergence at 10^3 realizations.

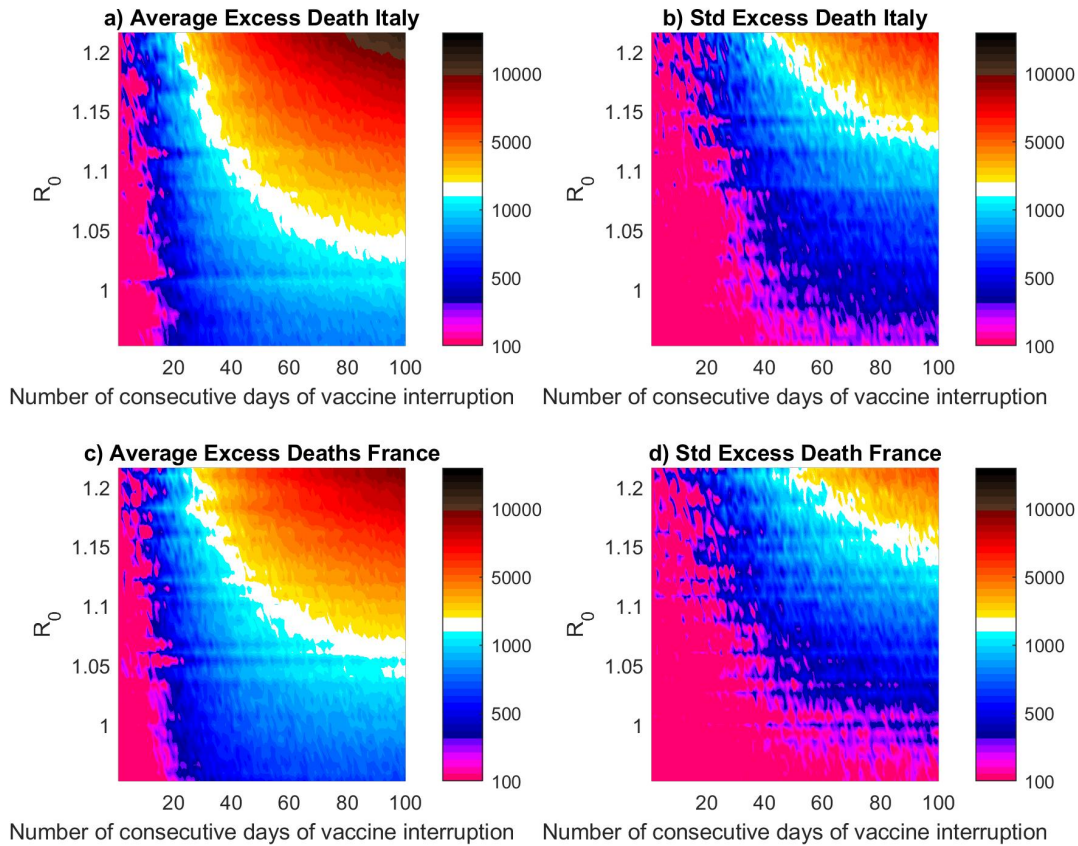


FIG. 3. (a,c) Average and (b,d) standard deviation over $N_r = 1000$ realizations of the stochastic SEIR model showing the excess deaths $m \times I(t)$ as a function of the number of the days of interruption of AstraZeneca vaccinations (x -axis) and R_0 (y -axis) for Italy (a,b) and France (c,d). The excess deaths are computed with respect to a base scenario where vaccine injections are never interrupted. With respect to Figure 2 in the main text, here the vaccination rate is doubled for a number of days equivalent to those of interruption. Note that x -axis starts at $N = 1$. Each realization of the SEIR model is integrated for 500 days.