The impact of COVID-19 vaccines on the Case Fatality Rate: The importance of monitoring breakthrough infections

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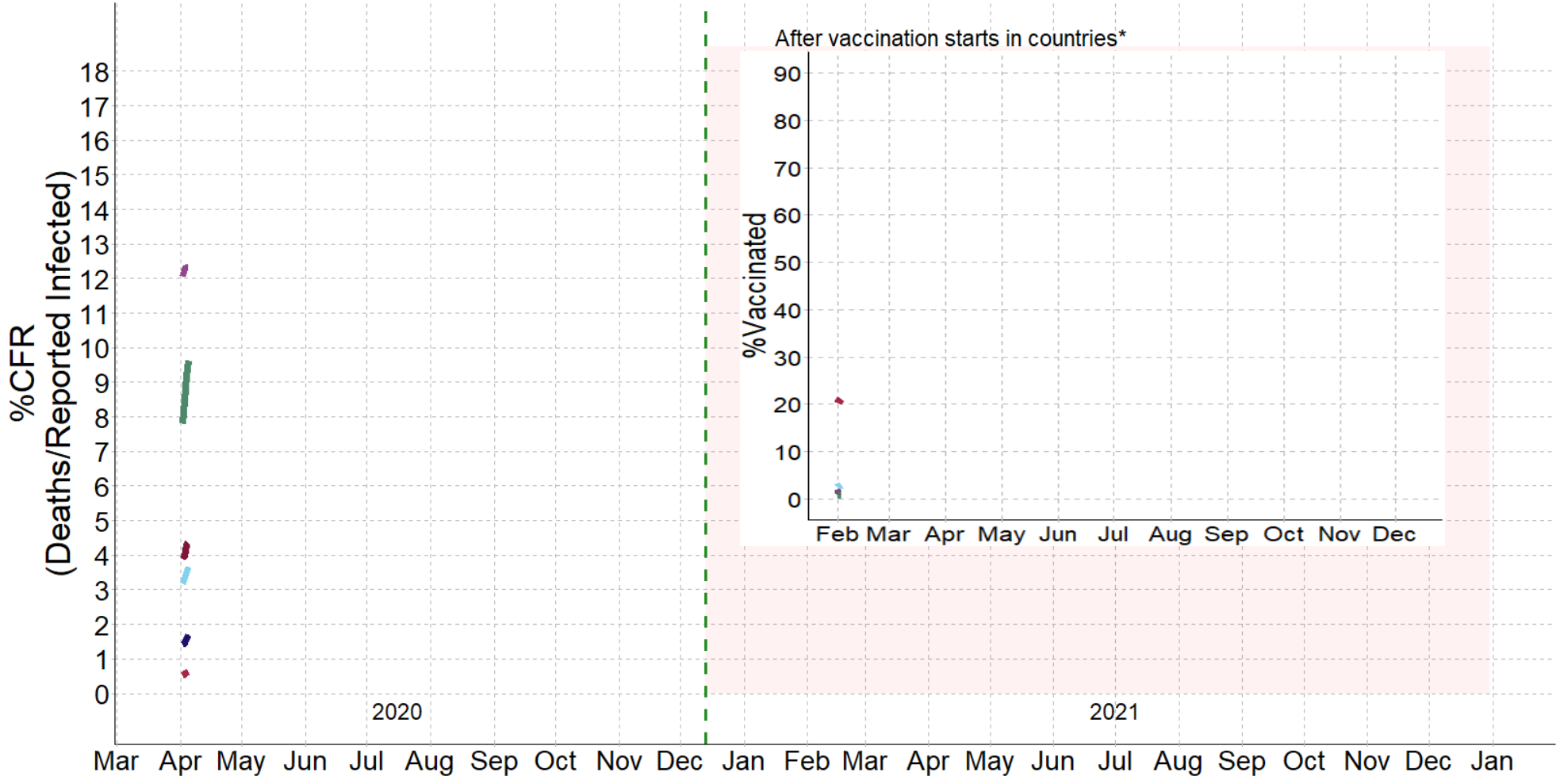
Fig. 1 Case Fatality Rate (CFR) and %Fully Vaccinated Trajectories



Source: Our World in Data (Mathieu et al. 2021)

What is driving this pattern in the CFR?

Are vaccines not being effective in reducing deaths?

The CFR is particularly sensitive to [1]:

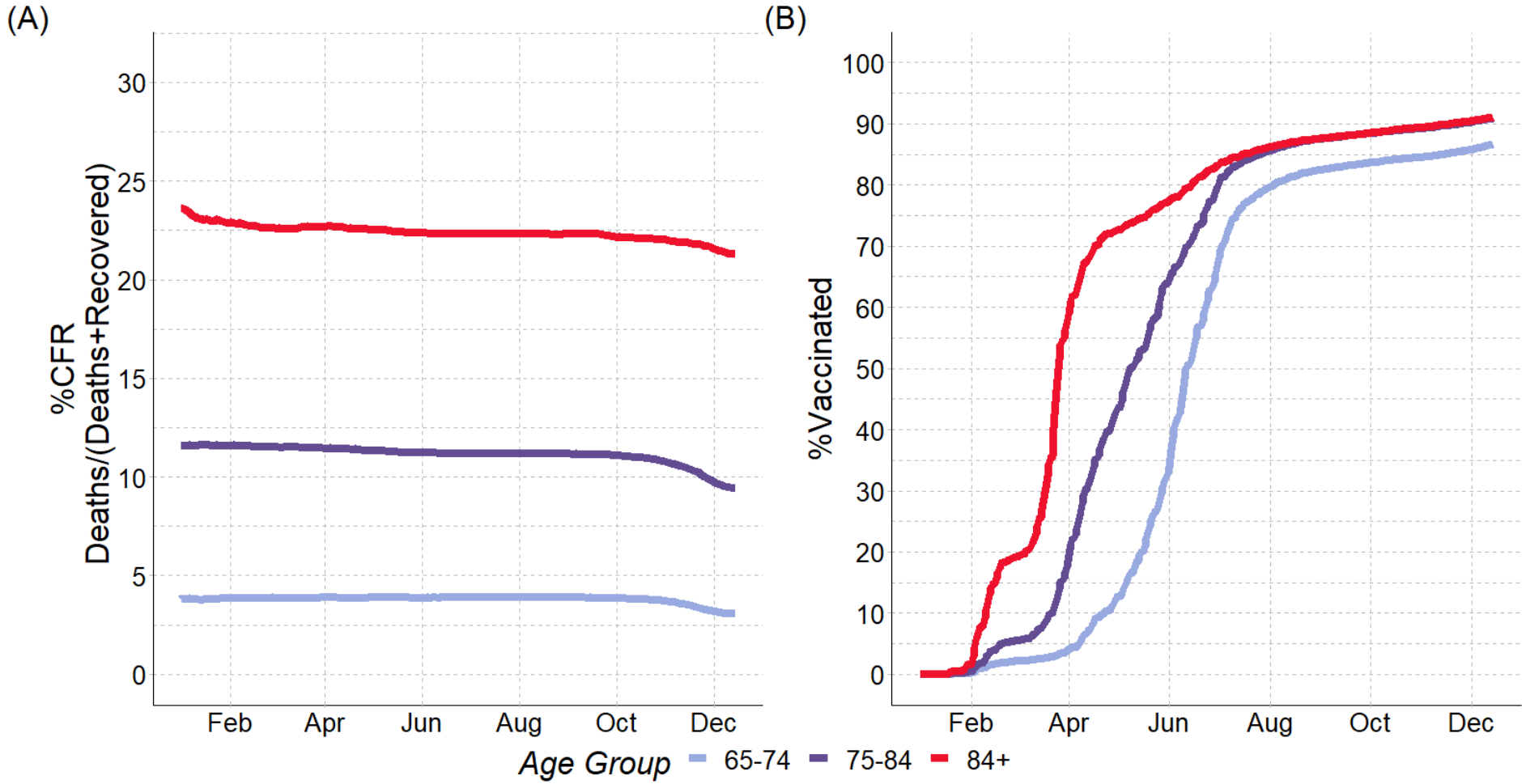
$$\text{CFR}_{t,a} = \frac{\text{Deaths}_{t,a}}{\text{Reported Cases}_{t,a}}$$

Any factor that impacts the number of confirmed deaths from a disease and the number of reported cases in a given time

- demographic factors
- delays in reported cases
- testing policies

[1] (Dowd et al. 2020; Rajgor et al. 2020; Goldstein and Lee 2020; Green et al. 2020; Harman et al. 2021; Smith 2021; Luo et al. 2021; Undurraga et al. 2021)

Fig. 2 Panel (A) %Case-Fatality Rate (CFR); Panel (B) Share of fully vaccinated persons (%). Austria, by age, from Jan to Dec 2021



Source: The number of people vaccinated at each group is taken from BMSGPK, Österreichisches COVID-19 Open Data Informationsportal (2021)

$$\mathrm{CFR}_{t,a} = \frac{\mathcal{D}^U_{t,a} + \mathcal{D}^V_{t,a}}{d^U_{t,a}\mathcal{I}^U_{t,a} + d^V_{t,a}\mathcal{I}^V_{t,a}} = \mathrm{CFR}^U_{t,a}(1 - \gamma_{t,a}) + \mathrm{CFR}^V_{t,a}\gamma_{t,a}$$

$\mathrm{CFR}_{t,a}$ being the weighted sum of $\mathrm{CFR}^U_{t,a}$ and $\mathrm{CFR}^V_{t,a}$ with weights $\gamma_{t,a}$:

$$\gamma_{t,a} = \frac{d^V_{t,a}\mathcal{I}^V_{t,a}}{d^U_{t,a}\mathcal{I}^U_{t,a} + d^V_{t,a}\mathcal{I}^V_{t,a}}$$

the ratio between the total number of COVID vaccine breakthroughs and the total number of COVID-associated ever infected and detected cases

$$\mathrm{CFR}_{t,a} = \mathrm{CFR}^{U}_{t,a}(1 - \gamma_{t,a}) + \mathrm{CFR}^{V}_{t,a}\gamma_{t,a}$$

$\gamma_{t,a} = 0$

$\gamma_{t,a} \neq 0$

No breakthrough cases:
$\mathrm{CFR}_{t,a} = \mathrm{CFR}^{U}_{t,a}$

How does $\mathrm{CFR}^{V}_{t,a}\gamma_{t,a}$ affect the $\mathrm{CFR}_{t,a}$?

$$\mathrm{CFR}^{V}_{t,a} = \mathrm{CFR}^{U}_{t,a} \frac{(1-\beta_a)}{Z_{t,a}}$$

$$(1-\beta_a) = Z_{t,a}$$

the CFR will remain **unchanged**, regardless the fact that the case fatality rate of the vaccinated is **lower** than the case fatality rate of the unvaccinated.

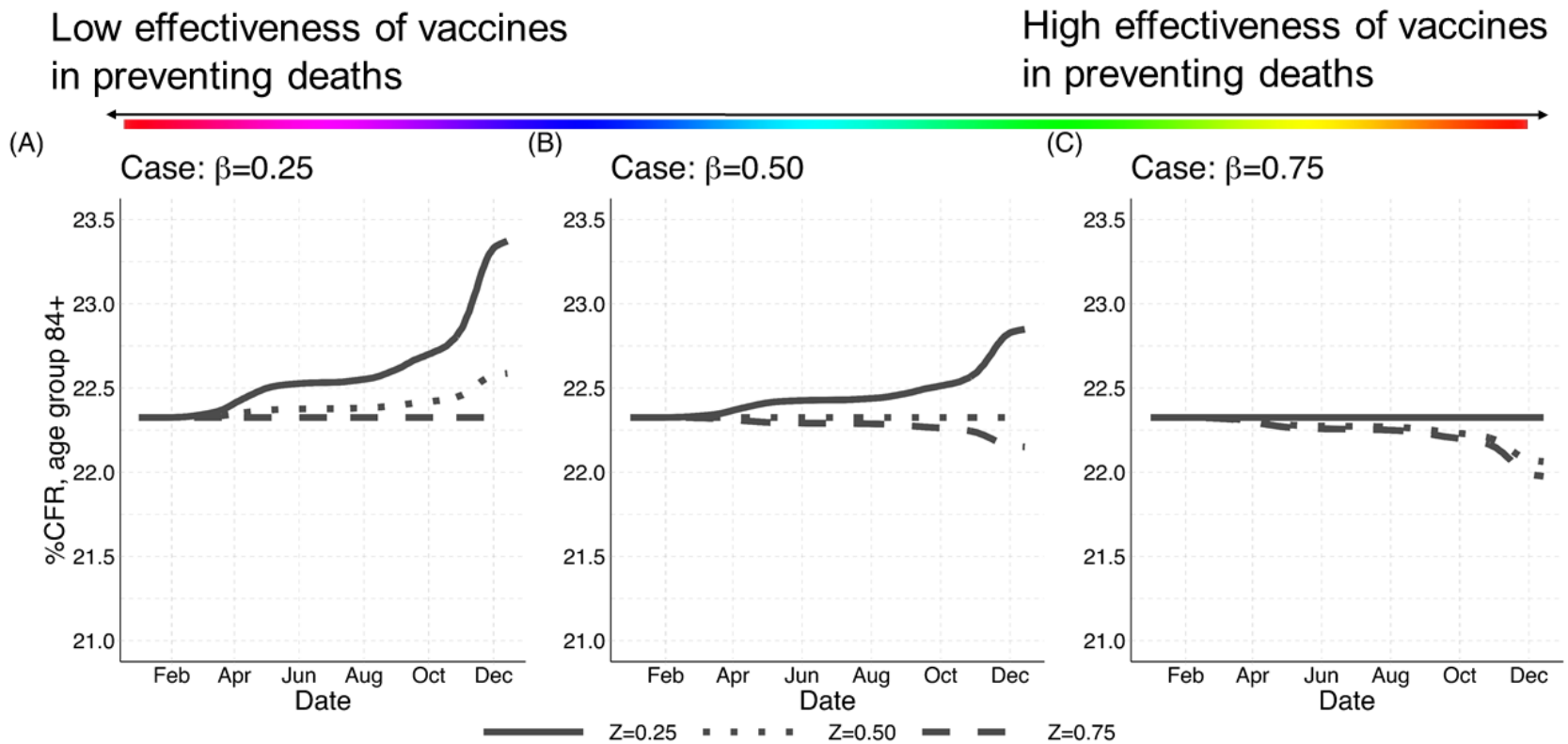
β_a = effectiveness of vaccines in preventing deaths

$Z_{t,a}$ = ratio of detection rates between the vaccinated and the unvaccinated

if $Z_{t,a} = 1$, the rate of detection among vaccinated and unvaccinated is the same

[2] Sánchez-Romero et al. 2021

Figure 3. Evolution of the %CFR for the age group 84+ in Austria (Jan-Dec 2021) by three different parameter values of $\beta_{(84+)}$ and $Z_{(t,84+)}$



Source: Simulated CFR values are calculated using data from (Richter et al. 2020b, a)and BMSGPK, COVID-19 Open Data Informationsportal (2021)

Conclusions

- A constant CFR can **still** mean that vaccines are effective in reducing deaths
- Detecting infections among both the vaccinated and unvaccinated population is key

Take-away: unless vaccinated people are **also** tested, it is hard to use the CFR as an indicator for monitoring the pandemic

Thank you for your attention!

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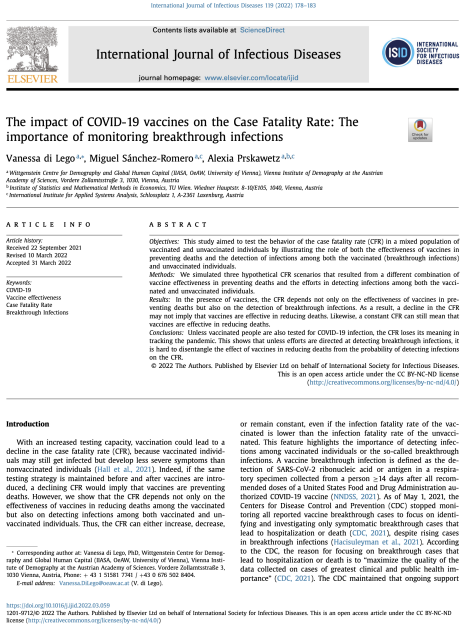

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The impact of COVID-19 vaccines on the Case Fatality Rate: The importance of monitoring breakthrough infections

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ABSTRACT

Objectives: This study aimed to test the behavior of the case fatality rate (CFR) in a mixed population of vaccinated and unvaccinated individuals by illustrating the role of both the effectiveness of vaccines in preventing deaths and the detection of infections among both the vaccinated (breakthrough infections) and unvaccinated individuals.
Methods: We simulated three hypothetical CFR scenarios that resulted from a different combination of vaccine effectiveness in preventing deaths and the efforts in detecting infections among both the vaccinated and unvaccinated individuals.
Results: In the presence of vaccines, the CFR depends not only on the effectiveness of vaccines in preventing deaths but also on the detection of breakthrough infections. As a result, a decline in the CFR may not imply that vaccines are effective in reducing deaths. Likewise, a constant CFR can still mean that vaccines are effective in reducing deaths.
Conclusions: Unless vaccinated people are also tested for COVID-19 infection, the CFR loses its meaning in tracking the pandemic. This shows that unless efforts are directed at detecting breakthrough infections, it is hard to disentangle the effect of vaccines in reducing deaths from the probability of detecting infections on the CFR.

Introduction

With an increased testing capacity, vaccination could lead to a decline in the case fatality rate (CFR), because vaccinated individuals may still get infected but develop less severe symptoms than nonvaccinated individuals (Hall et al., 2021). Indeed, if the same testing strategy is maintained before and after vaccines are introduced, a declining CFR would imply that vaccines are preventing deaths. However, we show that the CFR depends not only on the effectiveness of vaccines in reducing deaths among the vaccinated but also on detecting infections among both vaccinated and unvaccinated individuals. Thus, the CFR can either increase, decrease, or remain constant, even if the infection fatality rate of the vaccinated is lower than the infection fatality rate of the unvaccinated. This feature highlights the importance of detecting infections among vaccinated individuals or the so-called breakthrough infections. A vaccine breakthrough infection is defined as the detection of SARS-CoV-2 ribonucleic acid or antigen in a respiratory specimen collected from a person ≥14 days after all recommended doses of a United States Food and Drug Administration authorized COVID-19 vaccine (NNDSS, 2021). As of May 1, 2021, the Centers for Disease Control and Prevention (CDC) stopped monitoring all reported vaccine breakthrough cases to focus on identifying and investigating only symptomatic breakthrough cases that lead to hospitalization or death (CDC, 2021), despite rising cases in breakthrough infections (Harrisakeyman et al., 2021). According to the CDC, the reason for focusing on breakthrough cases that lead to hospitalization or death is to "maximize the quality of the data collected on cases of greatest clinical and public health importance" (CDC, 2021). The CDC maintained that ongoing support

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