Challenges in Estimating the Case Fatality Rate: Lessons from Demography

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Excess Deaths and Life-Years Lost Due to the Covid-19 Pandemic in Denmark
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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)

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Hence, one can decompose/split the CFR into two parts:

$$CFR_i - CFR_j = \alpha + \delta$$

with α being the age-structure of detected cases and δ the age-structure of case-fatality rates

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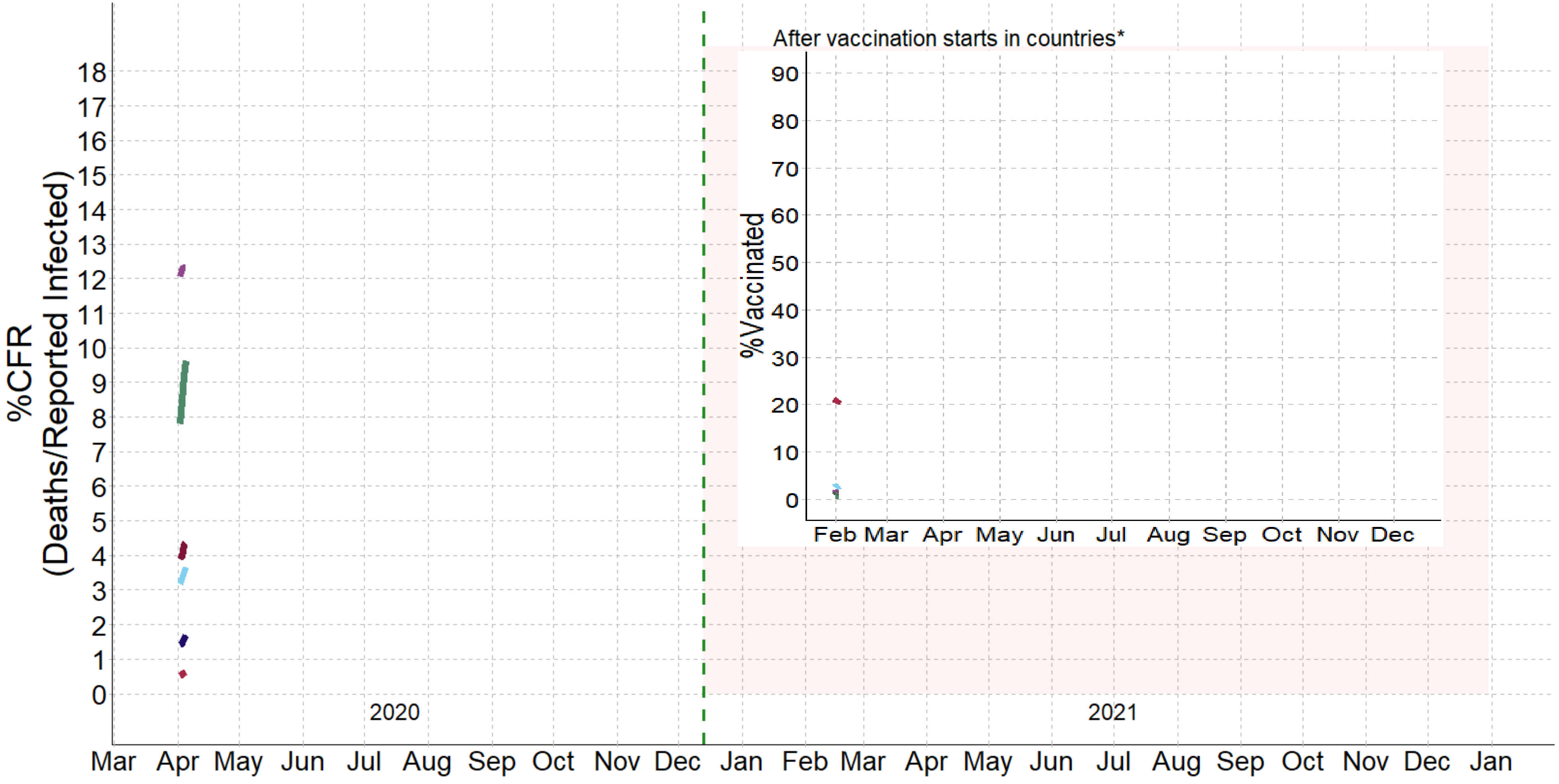
- the age-structure of detected cases α explained >60% of cross-country variation
- the age-structure of case-fatality rates δ within countries across time - mortality due to increasing age-specific case-fatality rates.]

[1] (Dudel C, Riffe T, Acosta E, van Raalte A, Strozza C, Myrskyla, M (2020))

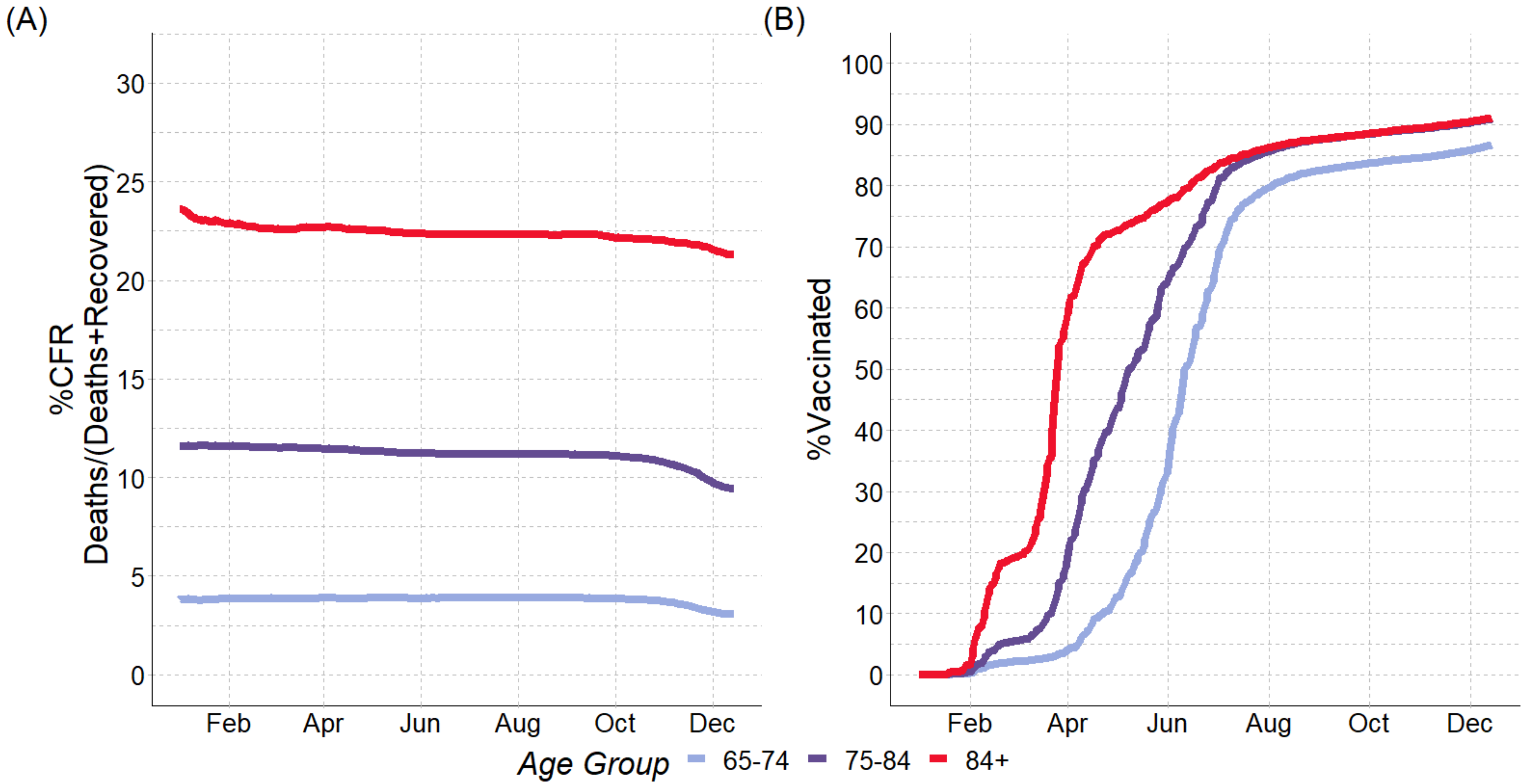
What happens in the presence of vaccines?

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



Source: Our World in Data (Mathieu 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)

What drives the patterns in the CFR in the presence of vaccines?

$$\mathrm{CFR}_{t,a} = \frac{\mathcal{D}^{U}_{t,a} + \mathcal{D}^{V}_{t,a}}{d^{U}_{t,a}\mathcal{I}^{U}_{t,a} + d^{V}_{t,a}\mathcal{I}^{V}_{t,a}}$$

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Let $m_a > 0$ be the COVID fatality rate for the age group a and $\beta_a \in (0,1)$ the effectiveness of vaccines in preventing deaths among the infected

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

Then, the fatality rate of the unvaccinated can be defined as m_a, while the fatality rate of the vaccinated becomes $m_a(1-\beta_a)$ (by definition smaller than m_a).

Let $m_a > 0$ be the COVID fatality rate for the age group a and $\beta_a \in (0,1)$ the effectiveness of vaccines in preventing deaths among the infected

Since the total number of deaths is given by the total number of infected times the associated fatality rate, we can rewrite $\mathrm{CFR}_{t,a}$ as:

$$\mathrm{CFR}_{t,a} = \frac{m_a \mathcal{I}_{t,a}^U + m_a (1-\beta_a) \mathcal{I}_{t,a}^V}{d_{t,a}^U \mathcal{I}_{t,a}^U + d_{t,a}^V \mathcal{I}_{t,a}^V}$$

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Taking m_a as common factor and multiplying and dividing by $d^U_{t,a}$ gives:

$$\text{CFR}_{t,a} = \frac{m_a}{d^U_{t,a}} \frac{d^U_{t,a}\mathcal{I}^U_{t,a} + (1-\beta_a) d^U_{t,a}\mathcal{I}^V_{t,a}}{d^U_{t,a}\mathcal{I}^U_{t,a} + d^V_{t,a}\mathcal{I}^V_{t,a}}$$

If we call $\gamma_{t,a} = d^V_{t,a}\mathcal{I}^V_{t,a}/(d^U_{t,a}\mathcal{I}^U_{t,a} + d^V_{t,a}\mathcal{I}^V_{t,a})$ the ratio between cases among the vaccinated and the total number of ever infected and detected cases, The case fatality rate can be rewritten as:

$$\mathrm{CFR}_{t,a} = \frac{m_a}{d^U_{t,a}}\left((1-\gamma_{t,a}) + (1-\beta_a)\frac{d^U_{t,a}}{d^V_{t,a}}\gamma_{t,a}\right)$$

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The value of $\gamma_{t,a} \in [0,1)$ will increase the higher is the number of cases among vaccinated individuals.

Denoting $Z_{t,a} = d^V_{t,a}/d^U_{t,a}$ as the proportion of detected cases among the ever infected after being vaccinated and the proportion detected among the ever infected and unvaccinated and substituting in the previous equation yields

$$\mathrm{CFR}_{t,a} = \frac{m_a}{d^U_{t,a}}\left((1-\gamma_{t,a}) + \frac{1-\beta_a}{Z_{t,a}}\gamma_{t,a}\right)$$

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or, alternatively:

$$\mathrm{CFR}_{t,a} = \mathrm{CFR}^U_{t,a}(1-\gamma_{t,a}) + \underbrace{\mathrm{CFR}^U_{t,a}\frac{1-\beta_a}{Z_{t,a}}\gamma_{t,a}}_{\mathrm{CFR}^V_{t,a}}$$

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This equation shows that the observed $\mathrm{CFR}_{t,a}$ is the weighted sum of the CFR of the unvaccinated $\mathrm{CFR}^U_{t,a} = m_a/d^U_{t,a}$ and the CFR of the vaccinated

$\mathrm{CFR}^V_{t,a} = (m_a/d^U_{t,a})((1-\beta_a)/Z_{t,a}) = m_a(1-\beta_a)/d^V_{t,a}$

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

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

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

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

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

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

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

No breakthrough cases:

$$\mathrm{CFR}_{t,a} = \mathrm{CFR}^{U}_{t,a}$$

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

$\gamma_{t,a} = 0$

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

No breakthrough cases:

$$\mathrm{CFR}_{t,a} = \mathrm{CFR}^{U}_{t,a}$$

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

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

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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

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

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

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.

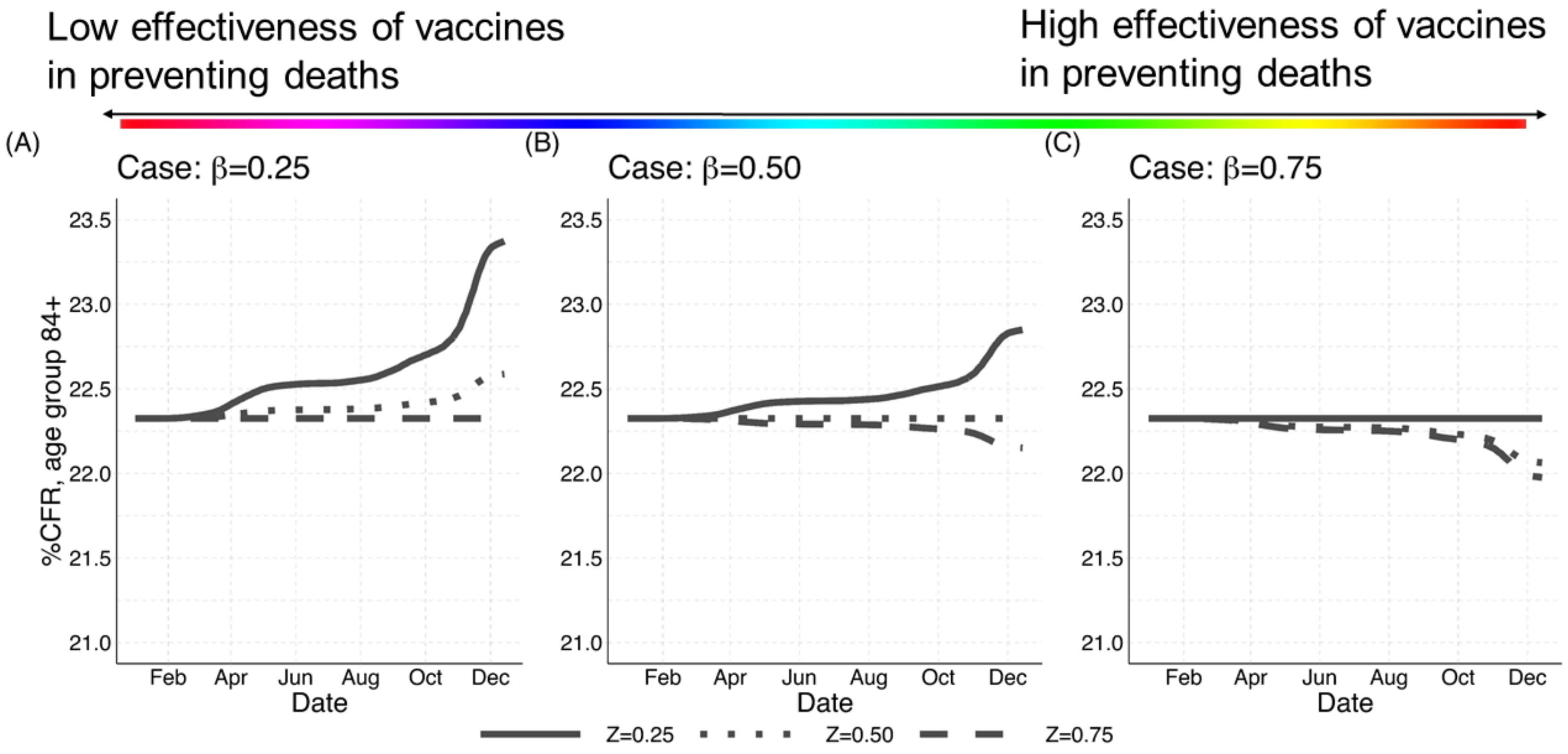
β_a = effectiveness of vaccines in preventing deaths

$Z_{t,a}$ = 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 $Z_{(t,84+)}$

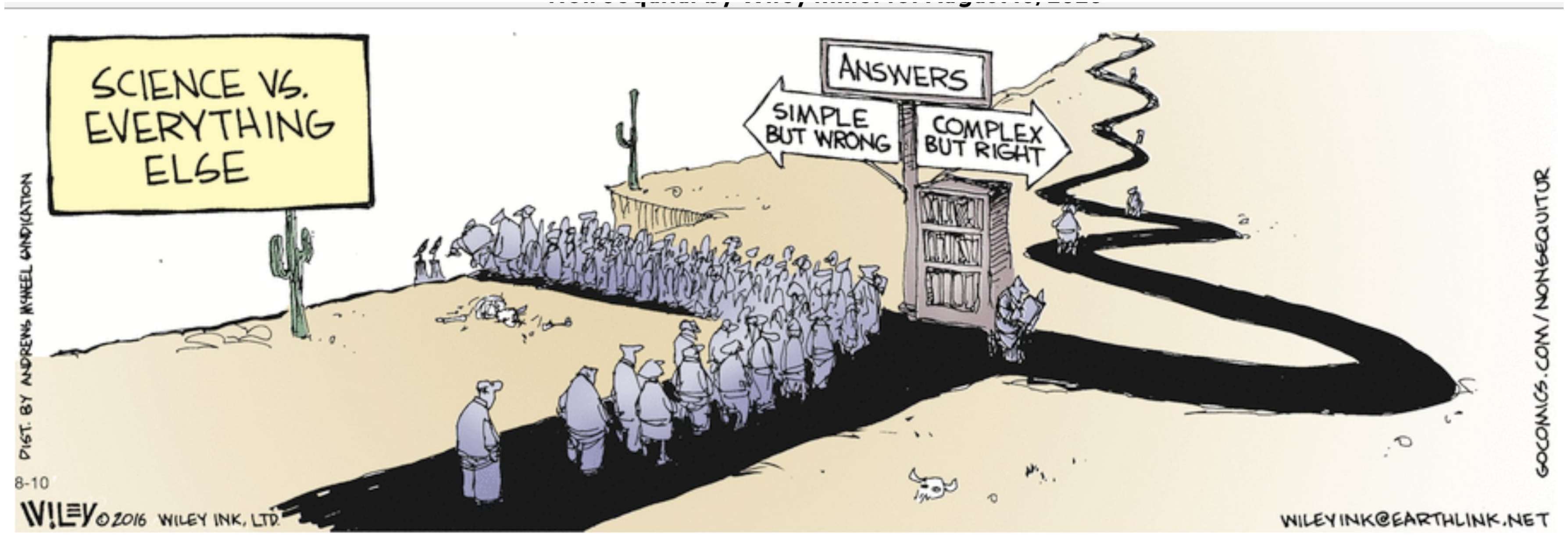


Source: Simulated CFR values are calculated using data from (Richter et al. 2020b, a)and BMSGPK, COVID-19 Open Data Informationsportal (2021), di Lego, V., Sánchez-Romero, M., Prskawetz, A. (2022). The impact of COVID-19 vaccines on the Case Fatality Rate: The importance of monitoring breakthrough infections. *International Journal of Infectious Diseases*,

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
- Unless vaccinated people are **also** tested, it is hard to use the CFR as an indicator for monitoring the pandemic
- However - CFR still useful measure for policy makers - how to improve/alternative measures
- Excess mortality also has its issues - maybe "temporary aging"?

Thank you!


SCIENCE VS. EVERYTHING ELSE
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COMPLEX BUT RIGHT
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