A Review of Excess Deaths:

A Critical Analysis of All-Cause Deaths During COVID-19 Vaccination in an Italian Province

Alberto Donzelli, MD

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Alberto Donzelli M.D. - Biography

Alberto Donzelli, born in Milan (Italy) in 1948, graduated in Medicine in 1973, specialist in Hygiene and Preventive Medicine and in Food Science.

I had a full-time professional career in Public Health, as Hygiene Service Manager and Health Director. Former member of the Italian Superior Council of Health.

Before retirement, for over a decade I directed the Appropriateness Education and Evidence Based Medicine Service of a large Italian Local Health Authority.

I am Author of hundreds of scientific publications (about sixty indexed on PubMed, and 9 on Embase), or of scientific dissemination.

I preside the *Allineare Sanità e Salute* Foundation, www.fondazioneallinearesanitaesalute.org, whose mission is to provide healthcare systems with research support and strategies to overcome the conflicts of interest with healthcare involving a growing number of healthcare players.

Coordinator of the Independent Medical-Scientific Commission (www.cmsindipendente.it)

Conflict of interests: none.

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Article

A Critical Analysis of All-Cause Deaths during COVID-19 Vaccination in an Italian Province

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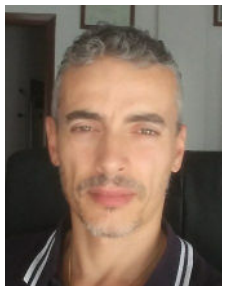
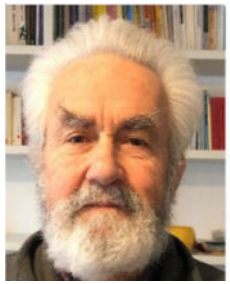

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vaccines

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MDPI

Article

COVID-19 Vaccination Effectiveness in the General Population of an Italian Province: Two Years of Follow-Up

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Abstract: (....)

found among the elderly: 22.0% of the unvaccinated, infected individuals died, as opposed to less than 3% of those who received greater than or equal to three vaccine doses. No protection against infection was observed, although this finding was certainly influenced by the Italian restriction policies to control the pandemic. Importantly, during the Omicron predominance period, only the group who received at least a booster dose showed a reduced risk of COVID-19-related death.

vaccines

The original study (University of Ferrara and Bologna)

MDPI

Article

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Table 3. Adjusted hazard ratios (HR; 95% confidence interval—CI) [A] of the outcomes of vaccination effectiveness, overall and by age category.

Outcomes	SARS-CoV-2	COVID-19 [B]	COVID-19-Related Death [B]	All-Cause Death
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Vaccine doses				
Unvaccinated	1 (Ref. cat.)	1 (Ref. cat.)	1 (Ref. cat.)	1 (Ref. cat.)
1 dose [C]	1.26 (1.21–1.32) *	0.47 (0.37–0.60) *	0.36 (0.28–0.47) *	1.40 (1.24–1.58) *
2 doses [D]	2.41 (2.37–2.46) *	0.27 (0.24–0.30) *	0.38 (0.32–0.44) *	1.36 (1.28–1.45) *
3/4 doses [E]	1.27 (1.25–1.29) *	0.12 (0.11–0.13) *	0.15 (0.14–0.17) *	0.22 (0.20–0.23) *

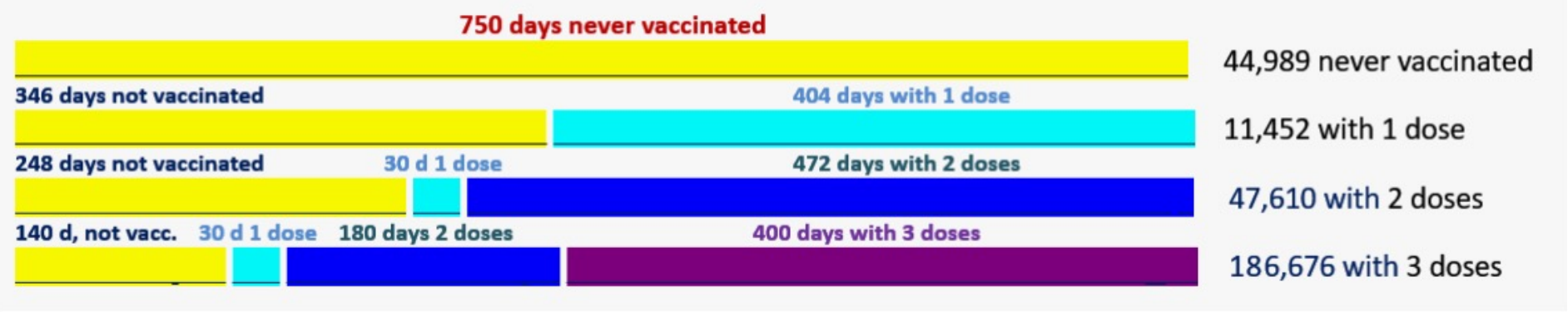
Compared to unvaccinated people, the authors reported a significant increase in all-cause mortality in people vaccinated with 1 or 2 doses,
but they insist that there is an important reduction in mortality with ≥3 doses, 4 times less (however, they did not correct for the *immortal-time bias*...!)

It is of paramount importance to correct for the *Immortal-time bias*, a systematic error that afflicts most observational studies on mortality from COVID-19 (and not only).

Indeed, the authors of the original study neglected that the "vaccinated"... for part of the observation-time were "**not** vaccinated"!
And that the people categorized as vaccinated with 2 or 3 doses spent a part of their observation-time in the previous status of 1 or 2 doses.

The correction of this bias reduces the denominator of people with ≥3 doses and, at the same time, the denominator of people in previous vaccination statuses increases, especially the one of the unvaccinated. Thus the number of deaths is diluted into a much larger denominator, and the rates are reduced.

Just to see an example of the functioning of this recalculation, see the simulation below.



EPIDEMIOLOGIA&PREVENZIONE – RIVISTA DELL'ASSOCIAZIONE ITALIANA DI EPIDEMIOLOGIA

e&P REPOSITORY

DOCUMENTI PREPRINT

[A reanalysis of an Italian study on the effectiveness of COVID-19 vaccination suggests that it might have unintended effects on total mortality - E&P Repository (epiprev.it)]

The authors of the Pescara study kept the commitment to give us the dataset, allowing us a multivariate analysis.
For this reason, this may be the more advanced study in the world, and it shows:

A reanalysis of an Italian study on the effectiveness of COVID-19 vaccination suggests that it might have unintended effects on total mortality

Publication date: 11/04/2024 – **E&P Code:** repo.epiprev.it/2862

Authors: Alessandria M.[1], Malatesta G.[2], Donzelli A.[3], Berrino F.[4].

SOTTOMESSO A E&P EPIDEMIOLOGIA & PREVENZIONE

Abstract: Immortal-time bias (ITB) is known to be common in cohort studies and distorts the association estimates between treated and untreated groups. We used data from the last of two large studies in an Italian province on COVID-19 vaccines safety and effectiveness incurred this bias, and aligned the entire population on a single index date, to correct the ITB. We considered the "all-cause deaths" outcome to compare the survival curves between the unvaccinated group and the various vaccination statuses. The all-cause deaths Hazard Ratios in univariate analysis for unvaccinated (reference) versus vaccinated with 1, 2, 3/4 doses were 0.88 (CI95: 0.78 –1.00; p-value 0.044), 1.23 (1.16–1.32; p-value ≤0.001) and 1.21 (1.14–1.29; p-value ≤0.001), respectively. The multivariate values were 2.40 (2.00–2.88; p-value <0.0001), 1.98 (1.75–2.24; p-value <0.0001), 0.99 (0.90–1.09; ns). The possible explanations of the trend of the Hazard Ratios as vaccinations increase could be a harvesting effect; a calendar-time bias, accounting for seasonality and pandemic waves; a case-counting windows bias; a healthy-vaccinee bias. Among their confirmations with two and even with 3/4 doses the calculated Restricted Mean Survival Time and Restricted Mean Time Lost have shown a small but significant downside for the vaccinated populations.

1st dose HR 2.40

2nd dose HR 1.98

3rd dose HR 0.99

Cite as: Alessandria M., Malatesta G., Donzelli A., Berrino F. (2024). A reanalysis of an Italian study on the effectiveness of COVID-19 vaccination suggests that it might have unintended effects on total mortality. E&P Repository https://repo.epiprev.it/2862

Topic: COVID-19

Key words: all-cause deaths, COVID-19 vaccines, Healthy-vaccinee bias, immortal-time bias.

HRs for people vaccinated with 2, or ≥3 doses may not be accurate, and for these two vaccination statuses we also calculated **Restricted Mean Survival Time** (RMSTs) and **Restricted Mean Time Lost** (RMTLs), comparing them to the same rates for the unvaccinated.

Differences in RMSTs between vaccinated and unvaccinated are significant for both the 2-dose and ≥3-dose groups.

They may seem irrelevant (a few days), but they refer to a limited period of time (739 days for those vaccinated with 2 doses, 579 days for those vaccinated with ≥3 doses).

Extrapolating the result to the entire life expectancy of the people of Pescara (82.6 years, i.e. 30,149 days; provided that e.g. US CDC recommend a yearly vaccination starting from 6 months), there would be an average loss in life expectancy:

- of ~3.6 months for those vaccinated with 2 doses
- by ~1.3 months for those vaccinated with ≥3 doses.

For reasons illustrated in our article, however, the loss of life expectancy for those who have been vaccinated several times could be greater.

Restricted Mean Survival Time (RMST) (τ=739 days o: in **~2 years**)

Groups	Estimate	SE	95% CI	
RMST 2-doses (arm1)	728.92	0.30	728.32 – 729.51	
RMST Unvaccianted (arm0)	731.62	0.18	731.27 – 731.98	
Restricted Mean Time Lost (RMTL)				
RMTL 2-doses (arm1)	10.08	0.30	9.49 – 10.67	
RMTL Unvaccianted (arm0)	7.37	0.18	7.01 – 7.73	
Between-group contrast				**p-value**
RMST (arm1-arm0) = days	**-2.7 days**		-3.40 – -2.01	<0.0001
RMTL (arm1/arm0) = approx HR	**1.37**		1.27 – 1.48	<0.0001

Table 3. Estimate of Restricted Mean Survival Time and Between-group contrast in 2-doses versus Unvaccinated.

Restricted Mean Survival Time (RMST) and **Restricted Mean Time Lost (RMTL)** are indices used to estimate respectively the **difference** and the **relationship between groups in terms of life expectancy**

In a survival analysis, they represent **the best statistical indices to interpret differences between groups** when the assumptions of the Cox Proportional model are not met[1].

1. *Rulli, E.; Ghilotti, F.; Biagioli, E.; Porcu, L.;. Assessment of proportional hazard assumption in aggregate data: a systematic review on statistical methodology in clinical trials using time-to-event endpoint. Br J Cancer. 2018 Dec;119(12):1456-1463. doi: 10.1038/s41416-018-0302-8.*

(*Elaboration by Dr. Marco Alessandria*)

Restricted Mean Survival Time (RMST) (τ=579 days o: in ~2 years)

Groups	Estimate	SE	95% CI	
RMST 3-doses (arm1)	573.68	0.11	573.46 – 573.89	
RMST Unvaccinated (arm0)	574.44	0.11	574.22 – 574.66	
Restricted Mean Time Lost (RMTL)				
RMTL 3-doses (arm1)	5.33	0.11	5.11 – 5.54	
RMTL Unvaccinated (arm0)	4.56	0.11	4.34 – 4.78	
Between-group contrast				p-value
RMST (arm1-arm0) = days	**-0.764**		-1.07 – -0.46	<0.0001
RMTL (arm1/arm0) = ~ HR	**1.17**		1.10 – 1.24	<0.0001

Table 4. Estimate of Restricted Mean Survival Time and Between-group contrast in 3-4 doses versus Unvaccinated.

The RMTL can approximate the HR in the absence of proportional hazard assumptions.[2]

The interpretation of these indices must be contextual to the interpretation of the HR in case of failure to satisfy the model assumptions.

2. *Uno, H.; Claggett, B.; Tian, L.; et al. Adding a new analytical procedure with clinical interpretation in the tool box of survival analysis. Ann Oncol. 2018;29(5):1092-1094.*

(*Elaboraz. Dr. Marco Alessandria*)

(4) Italian study calculates Covid-19 vaccine reduces average life expectancy by four months (substack.com)


Italian study calculates Covid-19 vaccine reduces average life expectancy by four months by adjusting for significant biases in observational data

MARTIN NEIL NORMAN FENTON APR 19, 2024

Background

One week ago, on 11th April, a pre-print paper appeared in the repository of "Epidemiology and Prevention", the in-house Journal of the Italian Association of Epidemiology. The

«Selection biases addressed and unaddressed

What makes this paper interesting and exciting is that, **unlike almost all observational studies of vaccine effectiveness and safety, two critical sources of bias are avoided**:

Immortal time bias (ITB) (…) and [**Confounding by indication**]

Conclusions

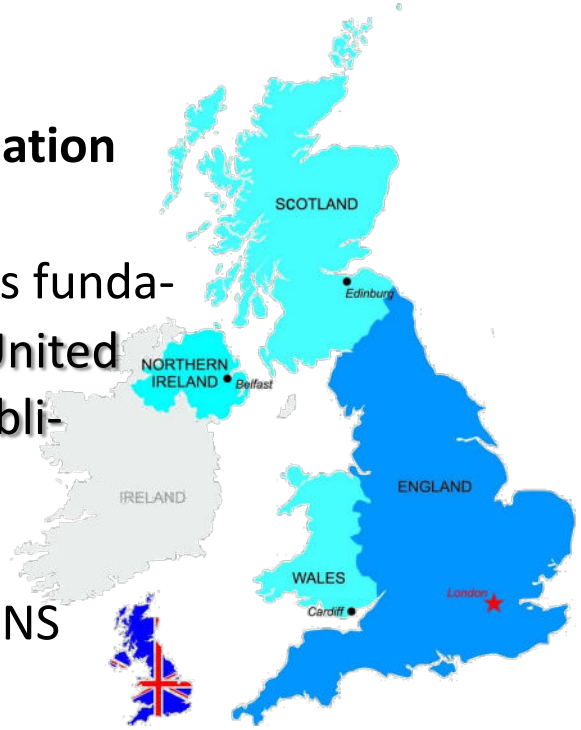
Even though the data suffers from the miscategorisation bias, as well as some other potential confounding effects, which they carefully note, **this is clearly the best quality study we have available on Covid-19 vaccination to date»**

What makes this research such an important advance? The fact that the results were achieved:

• using **all-cause mortality data broken down by vaccination status**.

In few parts of the world has data been presented in this fundamental way: the best-known example is data from the United Kingdom's Office for National Statistics (ONS), which published mortality data for England, divided by COVID-19 vaccination status,

with follow-up made public until May 2023, when the ONS (shockingly) announced it would stop publishing…!



• **correcting for the *Immortal-time bias***, a systematic error that afflicts most observational studies on mortality from COVID-19 (and not only).

Indeed, the authors of the original study neglected that the vaccinated... for part of the observation-time were **not** vaccinated!

• also correcting for the ***Confounding by indication bias*** to the best of the information currently available in the data set relating to the population analyzed, thanks to a multivariate analysis that took into account the pathologies individually present before of death.

This correction allows us to respond to the common objection also raised for example against the shocking data from the latest ONS publications, in which deaths in England have increasingly concentrated among those vaccinated, with percentages that dramatically exceed the percentages of the vaccinated English population.

It is utterly clear that this happens because the most fragile and sick subjects, who are therefore more exposed to death, would be vaccinated and revaccinated with priority!

On the contrary, our multivariate analysis did not confirm this common belief at all!

The Pescara research, allowing to correct the results by taking into account the pathologies of each of the deceased, denies the aforementioned justification:

in fact, in the **multivariate analysis** those **vaccinated with one dose** presented a Hazard Ratio (HR) of death of **2.40** (with confidence intervals of 2.00 to 2.88) compared to the unvaccinated, after adjustment for age and other confounding factors.

Those **vaccinated with two doses** showed an almost double HR of death: **1.98** (from 1.75 to 2.24), worsening the significant increase in mortality that the authors of the original research had also found after one and two doses, which they had not corrected for *Immortal-time bias*.

This correction also allowed us to refute **the implausible mortality reduction of more than four times that these authors attributed to subjects with 3 or more doses**. Indeed, those **vaccinated with boosters died at the same rate as those who were not vaccinated**, just with the correction of the aforementioned macroscopic systematic error.

More sophisticated analyzes on this last result have highlighted a small but significant loss of life expectancy even for those vaccinated with boosters.

Moreover, vaccination was not associated with benefit in chronically ill patients

Table 3. All-cause deaths and hazard ratios (HRs) according to vaccination status in univariate and multivariate analyses.

Covariate	1 Dose	2 Doses	3/4 Doses
	Multivariate	Multivariate	Multivariate
	HR (95% CI)	HR (95% CI)	HR (95% CI)
Groups	2.40 (2.00–2.88) **	1.98 (1.75–2.24) **	0.99 (0.90–1.09)
Hypertension	1.49 (1.23–1.82) **	/	1.24 (1.11–1.39) **
Diabetes	2.00 (1.60–2.49) **	1.74 (1.38–2.20) **	1.68 (1.48–1.90) **
CVD	1.60 (1.31–1.96) **	1.78 (1.44–2.20) **	1.86 (1.65–2.09) **
Kidney disease	1.77 (1.35–2.34) **	2.44 (1.84–3.24) **	2.47 (2.11–2.89) **
Cancer	/	/	/
Infection	/	/	/
Age	/	/	/
Sex	1.50 (1.27–1.78) **	/	1.37 (1.24–1.51) **
COPD	2.01 (1.56–2.60) **	2.89 (2.18–3.84) **	1.85 (1.59–2.15) **

HRs = hazard ratios; CI = Confidence Interval; ‡ p-value = 0.044; * significance with p-value ≤ 0.001; ** significance with p-value < 0.0001. The HRs indicated with "/" are the covariate stratified in order to correct the assumptions of the Proportional Cox Mode.

Supplement to: Rosenblum HG, Gee J, Liu R, et al. Safety of mRNA vaccines administered during the initial 6 months of the US COVID-19 vaccination programme: an observational study of reports to the VAERS and v-safe. ***Lancet Infect Dis* 2022**; published online March 7. https://doi.org/10.1016/S1473-3099(22)00054-8.

2)

Figure S1: Number of reports of death per day following vaccination, by manufacturer, to Vaccine Adverse Event Reporting System (VAERS)—December 14, 2020–June 14, 2021

*x-axis reports through 161 days since last dose.

Another methodological error is to ignore the so called **harvesting effect**:
id est, those who died after one dose cannot still die after subsequent doses…
(also refer to New Zealand data…)

LETTER TO THE EDITOR

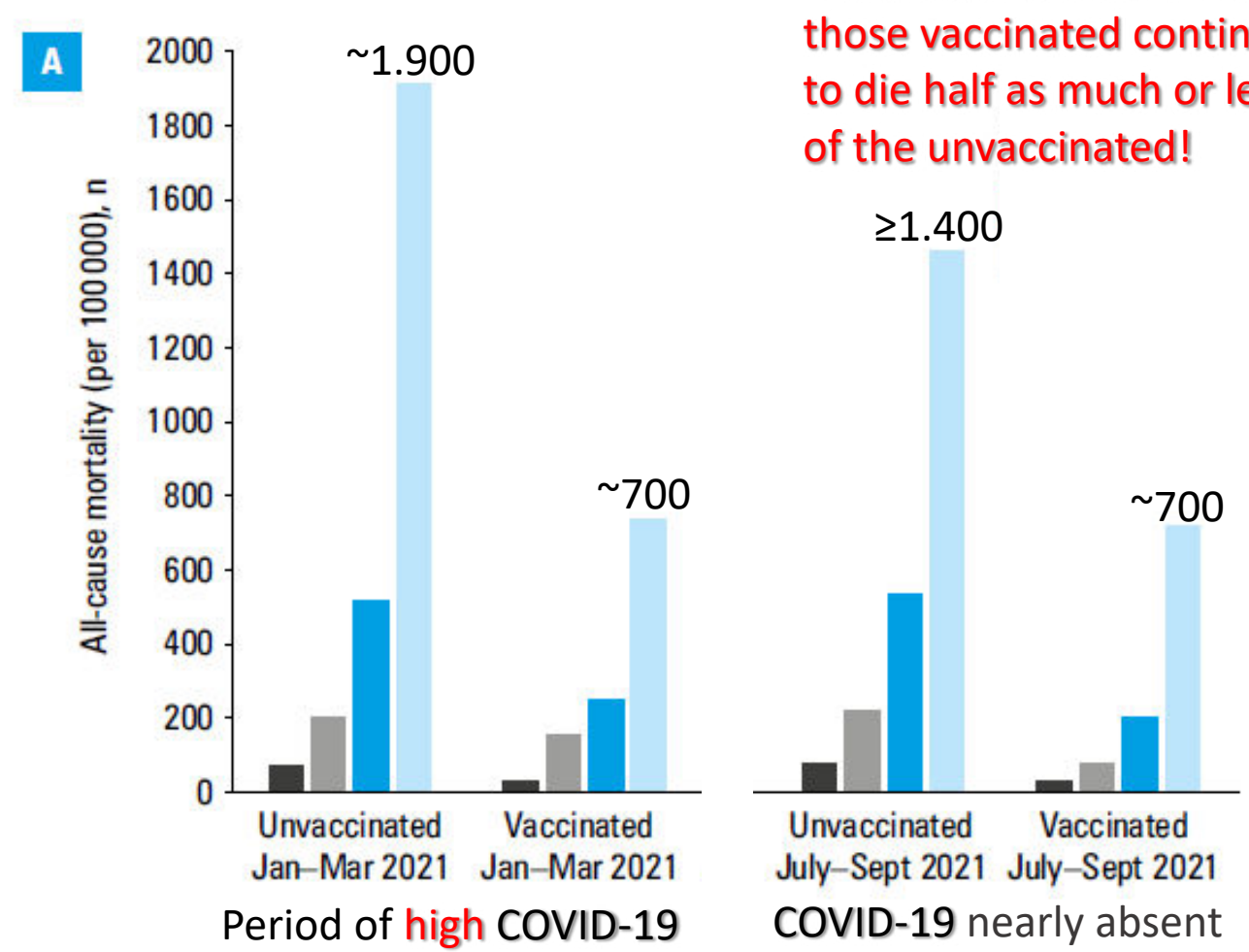
3) Healthy vaccinee effect: a bias not to be forgotten in observational studies on COVID-19 vaccine effectiveness - Polish Archives of Internal Medicine (mp.pl)

Healthy vaccinee effect: a bias not to be forgotten in observational studies on COVID-19 vaccine effectiveness

POLISH ARCH INTERN MED 2024; 134 (2)

Tomas Furst, Robert Straka, Jaroslav Janosek

Even without COVID-19 those vaccinated continue to die half as much or less of the unvaccinated!



Period of high COVID-19

COVID-19 nearly absent

A – all-cause mortality (ACM) in the vaccinated and unvaccinated populations in individual age groups during the high-COVID periods and very low-COVID

(health insurance data covering most of Czech Republic's population)

What explains the ***healthy-vaccinee bias***?

1 in the short term, those who have an indisposition (e.g. an acute respiratory infection) postpone vaccination; usually those who do it are fine at the moment

2) in the short (medium term): for those in the terminal phase, doctors or others can save the stress of a vaccination. But in this way their (probable) death will weigh heavily on the unvaccinated

3) from short to long term: people socio-economic disadvantaged, disabled and abandoned (and therefore more at risk of death) may have less access to vaccines

4) in the short-medium term: those who are more convinced of the effectiveness of a health intervention receive a **positive placebo effect** (the greater the more the intervention is presented in an *important* context/aura)

5) in the medium-long term: the more educated people adopt more prudent behaviors (driving, etc.) and seek better medical care (and therefore may be healthier), generally adhere more to vaccinations recommended by doctors, scientific societies, health authorities, *main stream* media

6) in the medium-long term: those who adhere to preventive interventions are more likely to adopt healthy lifestyles: diet, exercise, moderation in alcohol, no illegal drugs...: characteristics not evaluated in standard pharmaco-epidemiological databases, associated with fewer diseases/mortality in observational studies.

(PDF) The extent and impact of vaccine status miscategorisation on covid-19 vaccine efficacy studies (researchgate.net) **4) Cheap Trick** •DOI: 10.13140/RG.2.2.15216.67846

The extent and impact of vaccine status miscategorisation on covid-19 vaccine efficacy studies

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A systematic review of covid vaccine studies claiming high efficacy and/or safety

Simulation demonstrates that this miscategorisation bias artificially boosts vaccine efficacy and infection rates even when a vaccine has zero or negative efficacy. Furthermore, simulation demonstrates that repeated boosters, given every few months, are needed to maintain this misleading impression of efficacy. Given this, any claims of Covid-19 vaccine efficacy based on these studies are likely to be a statistical illusion.

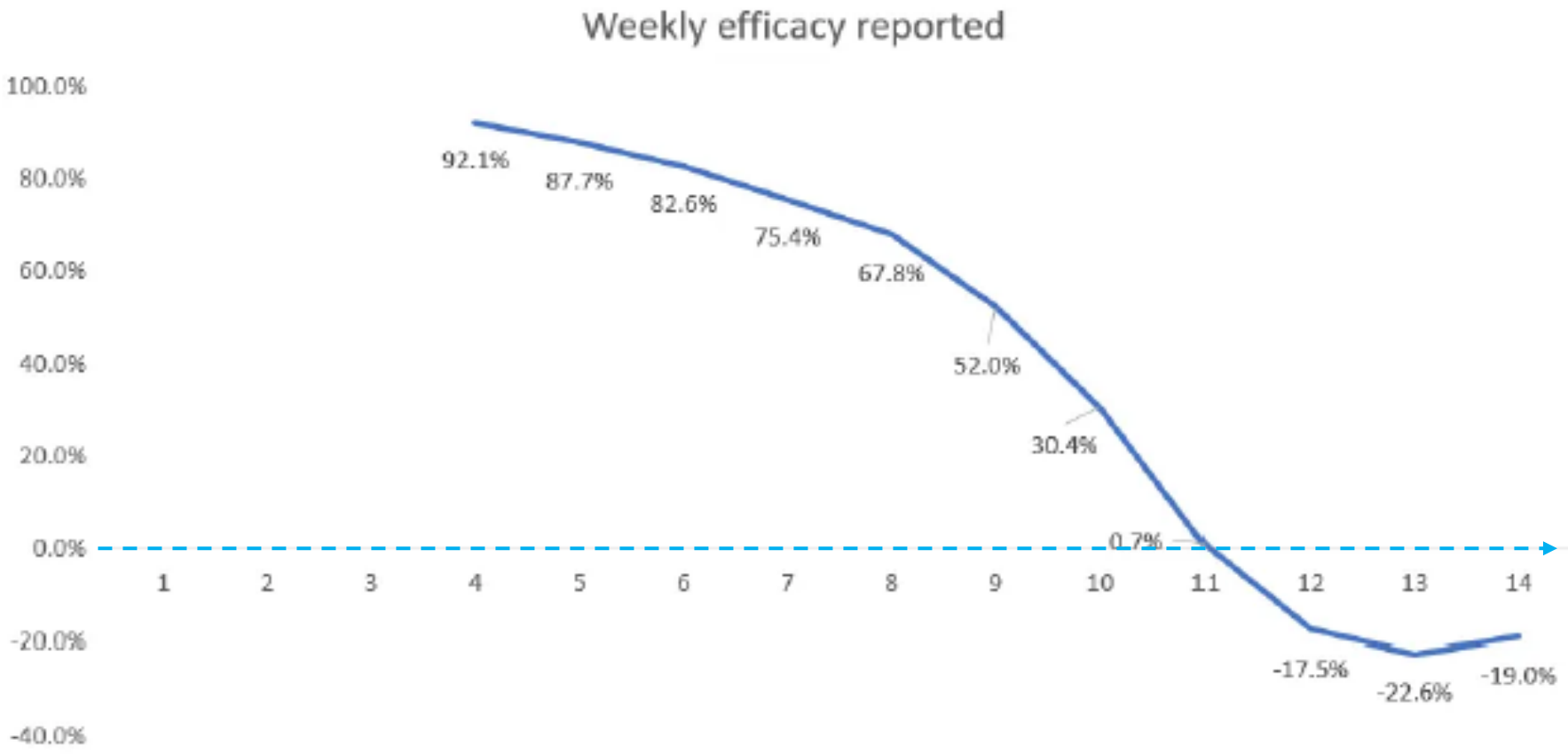
The mathematician and computer scientist Norman Fenton demonstrated that this 14 days shift creates a statistical illusion..

With the 14 day shift, a completely useless vaccine (with 0% true VE) appears to have very high VE in the first few weeks. While continuously decreasing, it is still above 50% at week 9. By week 14 the VE is still positive but only 12.1%... hence the need for a new booster dose!

These simulated results are very similar to the real-world VE rates seen in the first three months of a new vaccine or booster.

Even a negative VE can be made to appear >90% effective!

A placebo vaccine cannot truly achieve negative VE. But if the actual infection rate were a little higher for the vaccine than for no vaccine, the 14 (or 21) day rule still produces high initial efficacy, before it becomes negative.
Here is the simulation of the results for a vaccine that increases the infection rate by 50% in vaccinated people:



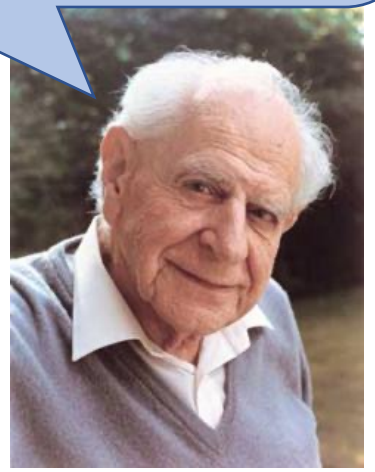
Conclusion

Due to the characteristics described, this research of ours is the one that those who want to continue with current vaccination policies should deal with.
I'm not saying we're necessarily right. We are men of science, trust the evidence, and we are open at least to these two possibilities:

- a demonstration that we have made methodological or calculation errors.
  We would be ready to recognize them publicly
- the presentation of one or more researchers 10 times larger, also extended into 2023, with similar characteristic of validity, but leading to opposite results.

In this case, however, our and other independent research groups should also be allowed to carry out verification analyzes on the same dataset.

A science that avoids dealing with its possible errors, immunizing itself against criticism to appear always true, **is not a science**



(Karl R. Popper, *La scienza, congetture e confutazioni*, in *Congetture e Confutazioni*, it., Bologna, Il Mulino, pp. 68-69)