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PRODUKTIE 6

Suriname Herald

Guyana schaft avondklok af, heeft geen effect op verspreiding COVID-19 gehad

13 februari 2022 om 12:19 Leestijd 1 minuut

President Irfaan Ali van Guyana

Guyana heeft de avondklok afgeschaft. Dit maakte de Guyanese regering bekend. President Mohamed Irfaan Ali zegt dat veel onderzoeken hebben aangetoond dat lockdowns en avondklokken weinig doen om de verspreiding van het COVID-19-virus in te dammen.

Bijna twee jaar nadat het COVID-19-virus Guyana in maart 2020 trof, is de avondklok die was ingesteld, eindelijk opgeheven in Guyana. De aankondiging

werd vrijdag met onmiddellijke ingang gedaan door de Nationale COVID-19 Task Force. Tot dusver heeft het land 1188 doden en 62.061 COVID-gevallen geregistreerd.

Daarnaast heeft de Guyanese Task Force aangekondigd dat alle zwembaden op 50 procent van hun capaciteit mogen draaien, maar alle zwemmers moeten volledig zijn ingeënt.

Niettegenstaande deze versoepelingen van de maatregelen, dringt de Task Force er bij alle Guyanezen op aan om verantwoordelijk gedrag te tonen.

VANDAAG

SURINAME

COVID-19: avondklok blijft gehandhaafd, feesten zijn verboden

BUITENLAND

Guyana schaft avondklok af, heeft geen effect op verspreiding COVID-19 gehad

SURINAME

Meer mogelijkheden door ICT voor inheemsen

Inheemsen uit de dorpen

PRODUKTIE 7

SAE./No.200/January 2022

Studies in Applied Economics

A LITERATURE REVIEW AND META-ANALYSIS OF THE EFFECTS OF LOCKDOWNS ON COVID-19 MORTALITY

Jonas Herby, Lars Jonung, and Steve H. Hanke

Johns Hopkins Institute for Applied Economics,
Global Health, and the Study of Business Enterprise

A Literature Review and Meta-Analysis of the Effects of Lockdowns on COVID-19 Mortality

By Jonas Herby, Lars Jonung, and Steve H. Hanke

About the Series

The *Studies in Applied Economics* series is under the general direction of Prof. Steve H. Hanke, Founder and Co-Director of The Johns Hopkins Institute for Applied Economics, Global Health, and the Study of Business Enterprise (hanke@jhu.edu). The views expressed in each working paper are those of the authors and not necessarily those of the institutions that the authors are affiliated with.

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Abstract

This systematic review and meta-analysis are designed to determine whether there is empirical evidence to support the belief that "lockdowns" reduce COVID-19 mortality. Lockdowns are defined as the imposition of at least one compulsory, non-pharmaceutical intervention (NPI). NPIs are any government mandate that directly restrict peoples' possibilities, such as policies that limit internal movement, close schools and businesses, and ban international travel. This study employed a systematic search and screening procedure in which 18,590 studies are identified that could potentially address the belief posed. After three levels of screening, 34 studies ultimately qualified. Of those 34 eligible studies, 24 qualified for inclusion in the meta-analysis. They were separated into three groups: lockdown stringency index studies, shelter-in-place-order (SIPO) studies, and specific NPI studies. An analysis of each of these three groups support the conclusion that lockdowns have had little to no effect on COVID-19 mortality. More specifically, stringency index studies find that lockdowns in Europe and the United States only reduced COVID-19 mortality by 0.2% on average. SIPOs were also ineffective, only reducing COVID-19 mortality by 2.9% on average. Specific NPI studies also find no broad-based evidence of noticeable effects on COVID-19 mortality.

While this meta-analysis concludes that lockdowns have had little to no public health effects, they have imposed enormous economic and social costs where they have been adopted. In consequence, lockdown policies are ill-founded and should be rejected as a pandemic policy instrument.

Acknowledgements

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Key Words: COVID-19, lockdown, non-pharmaceutical interventions, mortality, systematic review, meta-analysis

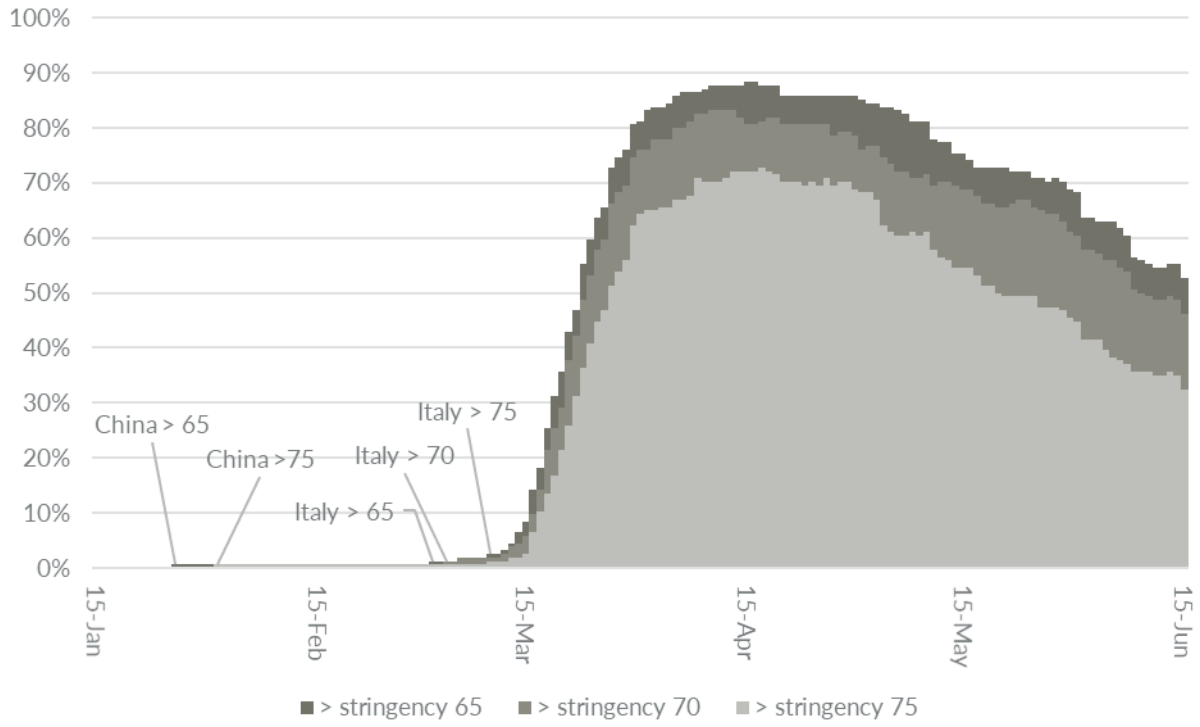
JEL Classification: I18; I38; D19

1 Introduction

The global policy reaction to the COVID-19 pandemic is evident. Compulsory non-pharmaceutical interventions (NPIs), commonly known as "lockdowns" – policies that restrict internal movement, close schools and businesses, and ban international travel – have been mandated in one form or another in almost every country.

The first NPIs were implemented in China. From there, the pandemic and NPIs spread first to Italy and later to virtually all other countries, see Figure 1. Of the 186 countries covered by the Oxford COVID-19 Government Response Tracker (OxCGRT), only Comoros, an island country in the Indian Ocean, did not impose at least one NPI before the end of March 2020.

Figure 1: Share of countries with OxCGRT stringency index above thresholds, January - June 2020



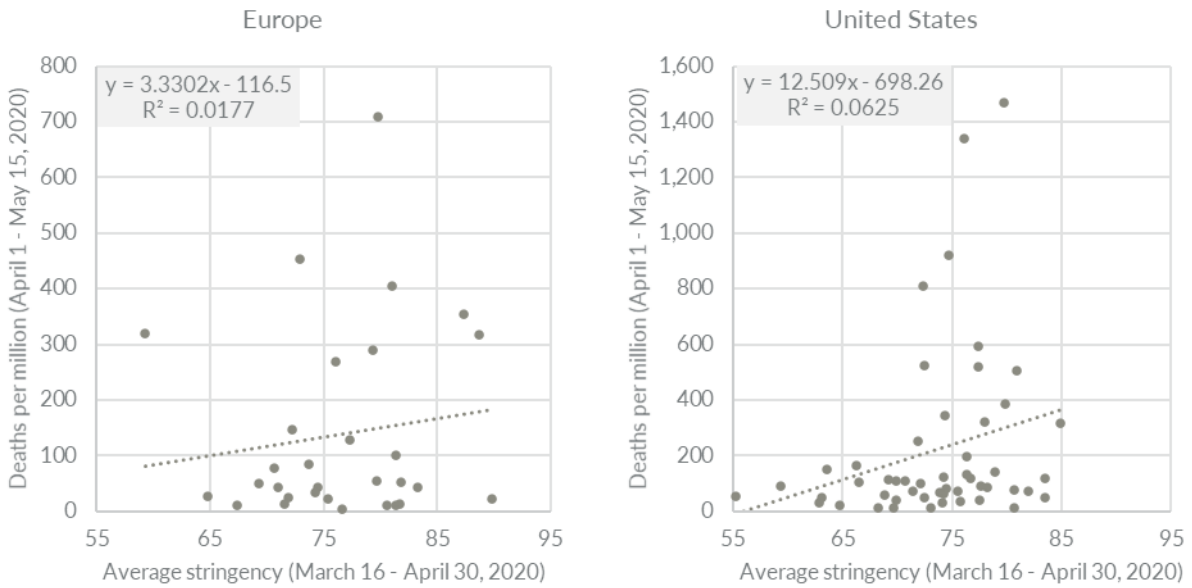
Comment: The figure shows the share of countries, where the OxCGRT stringency index on a given date surpassed index 65, 70 and 75 respectively. Only countries with more than one million citizens are included (153 countries in total). The OxCGRT stringency index records the strictness of NPI policies that restrict people's behavior. It is calculated using all ordinal containment and closure policy indicators (i.e., the degree of school and business closures, etc.), plus an indicator recording public information campaigns.
Source: Our World in Data.

Early epidemiological studies predicted large effects of NPIs. An often cited model simulation study by researchers at the Imperial College London (Ferguson et al. (2020)) predicted that a

suppression strategy based on a lockdown would reduce COVID-19 mortality by up to 98%.[1] These predictions were questioned by many scholars. Our early interest in the subject was spurred by two studies. First, Atkeson et al. (2020) showed that "across all countries and U.S. states that we study, the growth rates of daily deaths from COVID-19 fell from a wide range of initially high levels to levels close to zero within 20-30 days after each region experienced 25 cumulative deaths." Second, Sebhatu et al. (2020) showed that "government policies are strongly driven by the policies initiated in other countries," and less by the specific COVID-19-situation of the country.

A third factor that motivated our research was the fact that there was no clear negative correlation between the degree of lockdown and fatalities in the spring of 2020 (see Figure 2). Given the large effects predicted by simulation studies such as Ferguson et al. (2020), we would have expected to at least observe a simple negative correlation between COVID-19 mortality and the degree to which lockdowns were imposed.[2]

Figure 2: Correlation between stringency index and COVID-19 mortality in European countries and U.S. states during the first wave in 2020



Source: Our World in Data

[1] With R0 = 2.4 and trigger on 60, the number of COVID-19-deaths in Great Britain could be reduced to 8,700 deaths from 510,000 deaths (-98%) with a policy consisting of case isolation + home quarantine + social distancing + school/university closure, cf. Table 4 in Ferguson et al. (2020). R0 (the basic reproduction rate) is the expected number of cases directly generated by one case in a population where all individuals are susceptible to infection.

[2] In addition, the interest in this issue was sparked by the work Jonung did on the expected economic effects of the SARS pandemic in Europe in 2006 (Jonung and Röger, 2006). In this model-based study calibrated from Spanish flu data, Jonung and Röger concluded that the economic effects of a severe pandemic would be rather limited—a sharp contrast to the huge economic effects associated with lockdowns during the COVID-19 pandemic.

Today, it remains an open question as to whether lockdowns have had a large, significant effect on COVID-19 mortality. We address this question by evaluating the current academic literature on the relationship between lockdowns and COVID-19 mortality rates.[3] We use "NPI" to describe *any government mandate which directly restrict peoples' possibilities*. Our definition does *not* include governmental recommendations, governmental information campaigns, access to mass testing, voluntary social distancing, etc., but *do* include mandated interventions such as closing schools or businesses, mandated face masks etc. We define *lockdown* as any policy consisting of at least one NPI as described above.[4]

Compared to other reviews such as Herby (2021) and Allen (2021), the main difference in this meta-analysis is that we carry out a systematic and comprehensive search strategy to identify all papers potentially relevant to answer the question we pose. We identify 34 eligible empirical studies that estimate the effect of mandatory lockdowns on COVID-19 mortality using a counterfactual difference-in-difference approach. We present our results in such a way that they can be systematically assessed, replicated, and used to derive overall meta-conclusions.[5]

2 Identification process: Search strategy and eligibility criteria

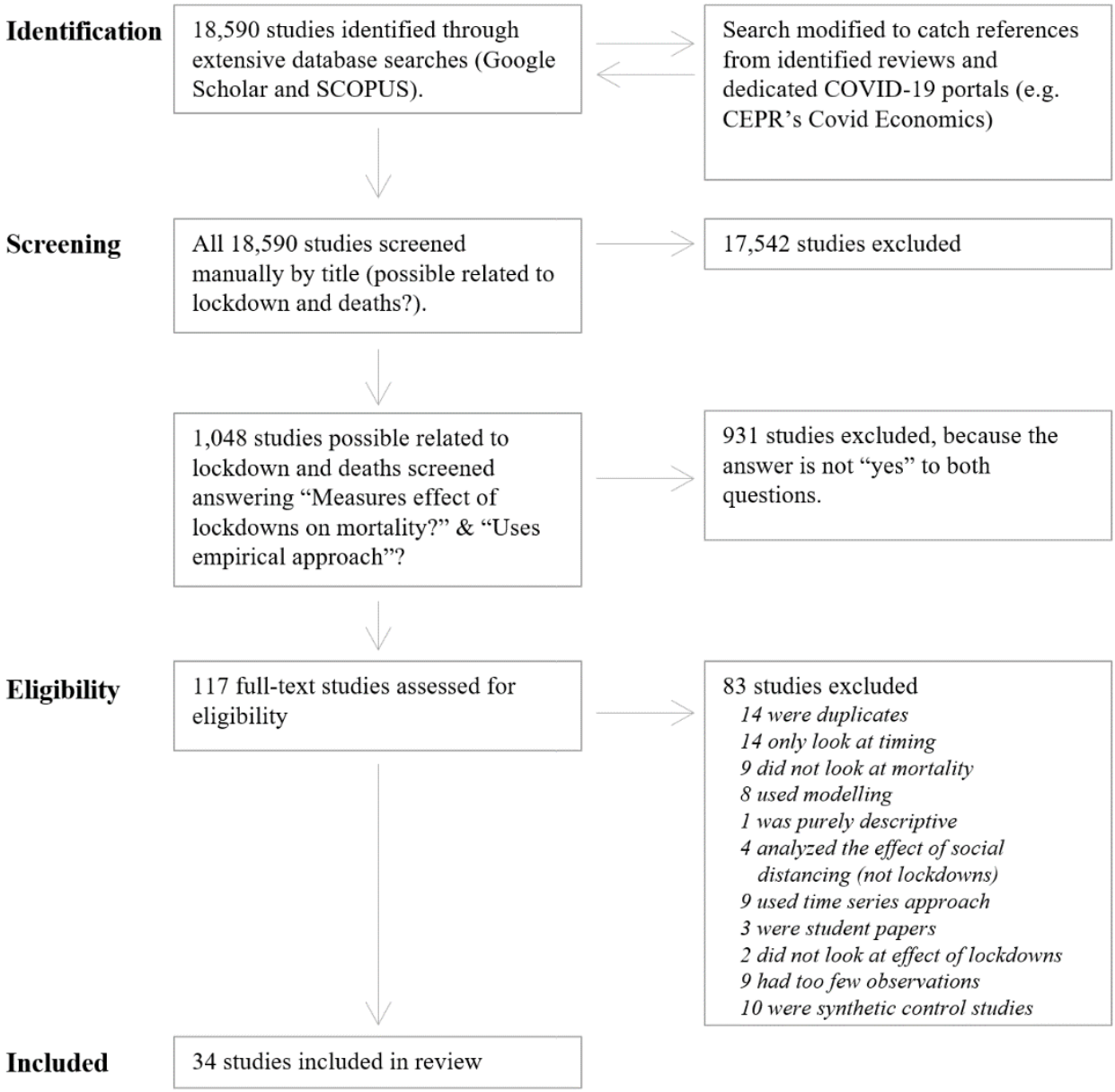
Figure 3 shows an overview of our identification process using a flow diagram designed according to PRISMA guidelines (Moher et al. (2009). Of 18,590 studies identified during our database searches, 1,048 remained after a title-based screening. Then, 931 studies were excluded, because they either did not measure the effect of lockdowns on mortality or did not use an empirical approach. This left 117 studies that were read and inspected. After a more thorough assessment, 83 of the 117 were excluded, leaving 34 studies eligible for our meta-analysis. A table with all 83 studies excluded in the final step can be found in Appendix B, Table 8.

[3] We use "mortality" and "mortality rates" interchangeably to mean COVID-19 deaths per population.

[4] For example, we will say that Country A introduced the *non-pharmaceutical interventions* school closures and shelter-in-place-orders as part of the country's *lockdown*.

[5] An interesting question is, "What damage lockdowns do to the economy, personal freedom and rights, and public health in general?" Although this question is important, it requires a full cost-benefit study, which is beyond the scope of this study.

Figure 3: PRISMA flow diagram for the selection of studies.



Below we present our search strategy and eligibility criteria, which follow the PRISMA guidelines and are specified in detail in our protocol Herby et al. (2021).

2.1 Search strategy

The studies we reviewed were identified by scanning *Google Scholar* and *SCOPUS* for English-language studies. We used a wide range of search terms which are combinations of three search strings: a disease search string ("covid," "corona," "coronavirus," "sars-cov-2"), a government

response search string[6], and a methodology search string[7]. We identified papers based on 1,360 search terms. We also required mentions of "deaths," "death," and/or "mortality." The search terms were continuously updated (by adding relevant terms) to fit this criterion.[8]

We also included all papers published in *Covid Economics*. Our search was performed between July 1 and July 5, 2021 and resulted in 18,590 unique studies.[9] All studies identified using SCOPUS and Covid Economics were also found using Google Scholar. This made us comfortable that including other sources such as VOXeu and SSRN would not change the result. Indeed, many papers found using Google Scholar were from these sources.

All 18,590 studies were first screened based on the title. Studies clearly not related to our research question were deemed irrelevant.[10]

After screening based on the title, 1,048 papers remained. These papers were manually screened by answering two questions:

1. Does the study measure the effect of lockdowns on mortality?
2. Does the study use an empirical *ex post* difference-in-difference approach (see eligibility criteria below)?

Studies to which we could not answer "yes" to both questions were excluded. When in doubt, we made the assessment based on reading the full paper, and in some cases, we consulted with colleagues.[11]

After the manual screening, 117 studies were retrieved for a full, detailed review. These studies were carefully examined, and metadata and empirical results were stored in an Excel

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[6] The government response search string used was: "non-pharmaceutical," "nonpharmaceutical," "NPI," "NPIs," "lockdown," "social distancing orders," "statewide interventions," "distancing interventions," "circuit breaker," "containment measures," "contact restrictions," "social distancing measures," "public health policies," "mobility restrictions," "covid-19 policies," "corona policies," "policy measures."

[7] The methodology search string used was: ("fixed effects," "panel data," "difference-in-difference," "diff-in-diff," "synthetic control," "counterfactual" , "counter factual," "cross country," "cross state," "cross county," "cross region," "cross regional," "cross municipality," "country level," "state level," "county level," "region level," "regional level," "municipality level," "event study."

[8] If a potentially relevant paper from one of the 13 reviews (see eligibility criteria) did not show up in our search, we added relevant words to our search strings and ran the search again. The 13 reviews were: Allen (2021); Brodeur et al. (2021); Gupta et al. (2020); Herby (2021); Johanna et al. (2020); Nussbaumer-Streit et al. (2020); Patel et al. (2020); Perra (2020); Poeschl and Larsen (2021); Pozo-Martin et al. (2020); Rezapour et al. (2021); Robinson (2021); Zhang et al. (2021).

[9] SCOPUS was continuously monitored between July 5th and publication using a search agent. Although the search agent returned several hits during this period, only one of them, An et al. (2021), was eligible according to our eligibility criteria. The study is not included in our review, but the conclusions are in line with our conclusions, as An et al. (2021) conclude that "The analysis shows that the mask mandate is consistently associated with lower infection rates in the short term, and its early adoption boosts the long-term efficacy. By contrast, the other five policy instruments— domestic lockdowns, international travel bans, mass gathering bans, and restaurant and school closures—show weaker efficacy."

[10] This included studies with titles such as "COVID-19 outbreak and air pollution in Iran: A panel VAR analysis" and "Dynamic Structural Impact of the COVID-19 Outbreak on the Stock Market and the Exchange Rate: A Cross-country Analysis Among BRICS Nations."

[11] Professor Christian Bjørnskov of University of Aarhus was particularly helpful in this process.

spreadsheet. All studies were assessed by at least two researchers. During this process, another 64 papers were excluded because they did not meet our eligibility criteria. Furthermore, nine studies with too little jurisdictional variance (< 10 observations) were excluded,[12] and 10 synthetic control studies were excluded.[13] A table with all 83 studies excluded in the final step can be found in Appendix B, Table 8. Below we explain why these studies are excluded.

2.2 Eligibility criteria

Focus on mortality and lockdowns

We only include studies that attempt to establish a relationship (or lack thereof) between lockdown policies and COVID-19 mortality or excess mortality. We exclude studies that use cases, hospitalizations, or other measures.[14]

Counterfactual difference-in-difference approach

We distinguish between two methods used to establish a relationship (or lack thereof) between mortality rates and lockdown policies. The first uses registered cross-sectional mortality data. These are *ex post* studies. The second method uses simulated data on mortality and infection rates.[15] These are *ex ante* studies.

We include all studies using a counterfactual difference-in-difference approach from the former group but disregard all *ex ante* studies, as the results from these studies are determined by model assumptions and calibrations.

Our limitation to studies using a "counterfactual difference-in-difference approach" means that we exclude all studies where the counterfactual is based on forecasting (such as a SIR-model) rather than derived from a difference-in-difference approach. This excludes studies like Duchemin et al. (2020) and Matzinger and Skinner (2020). We also exclude all studies based on interrupted time series designs that simply compare the situation before and after lockdown, as

[12] The excluded studies with too few observations were: Alemán et al. (2020), Berardi et al. (2020), Conyon et al. (2020a), Coccia (2021), Gordon et al. (2020), Juranek and Zoutman (2021), Kapoor and Ravi (2020), Umer and Khan (2020), and Wu and Wu (2020).

[13] The excluded synthetic control studies were: Conyon and Thomsen (2021), Dave et al. (2020), Ghosh et al. (2020), Born et al. (2021), Reinbold (2021), Cho (2020), Friedson et al. (2021), Neidhöfer and Neidhöfer (2020), Cerqueti et al. (2021), and Mader and Rüttenauer (2021).

[14] Analyses based on cases may pose major problems, as testing strategies for COVID-19 infections vary enormously across countries (and even over time within a given country). In consequence, cross-country comparisons of cases are, at best, problematic. Although these problems exist with death tolls as well, they are far more limited. Also, while cases and death tolls are correlated, there may be adverse effects of lockdowns that are not captured by the number of cases. For example, an infected person who is isolated at home with family under a SIPO may infect family members with a higher viral load causing more severe illness. So even if a SIPO reduces the number of cases, it may theoretically increase the number of COVID-19-deaths. Adverse effects like this may explain why studies like Chernozhukov et al. (2021) finds that SIPO reduces the number of cases but have no significant effect on the number of COVID-19-deaths. Finally, mortality is hierarchically the most important outcome, cf. GRADEpro (2013)

[15] These simulations are often made in variants of the SIR-model, which can simulate the progress of a pandemic in a population consisting of people in different states (Susceptible, Infectious, or Recovered) with equations describing the process between these states.

the effect of lockdowns in these studies might contain time-dependent shifts, such as seasonality. This excludes studies like Bakolis et al. (2021) and Siedner et al. (2020).

Given our criteria, we exclude the much-cited paper by Flaxman et al. (2020), which claimed that lockdowns saved three million lives in Europe. Flaxman et al. assume that the pandemic would follow an epidemiological curve unless countries locked down. However, this assumption means that the only interpretation possible for the empirical results is that lockdowns are the only thing that matters, even if other factors like season, behavior etc. caused the observed change in the reproduction rate, Rt. Flaxman et al. are aware of this and state that "our parametric form of R_t assumes that changes in Rt are an immediate response to interventions rather than gradual changes in behavior." Flaxman et al. illustrate how problematic it is to force data to fit a certain model if you want to infer the effect of lockdowns on COVID-19 mortality.[16]

The counterfactual difference-in-difference studies in this review generally exploit variation across countries, U.S. states, or other geographical jurisdictions to infer the effect of lockdowns on COVID-19 fatalities. Preferably, the effect of lockdowns should be tested using randomized control trials, natural experiments, or the like. However, there are very few studies of this type.[17]

Synthetic control studies

The synthetic control method is a statistical method used to evaluate the effect of an intervention in comparative case studies. It involves the construction of a synthetic control which functions as the counter factual and is constructed as an (optimal) weighted combination of a pool of donors. For example, Born et al. (2021) create a synthetic control for Sweden which consists of 30.0% Denmark, 25.3% Finland, 25.8% Netherlands, 15.0% Norway, and 3.9% Sweden. The effect of the intervention is derived by comparing the actual developments to those contained in the synthetic control.

We exclude synthetic control studies because of their inherent empirical problems as discussed by Bjørnskov (2021b). He finds that the synthetic control version of Sweden in Born et al. (2021) deviates substantially from "actual Sweden," when looking at the period before mid-March 2020, when Sweden decided not to lock down. Bjørnskov estimates that *actual Sweden* experienced

[16] Several scholars have criticized Flaxman et al. (2020), e.g. see Homburg and Kuhbandner (2020), Lewis (2020), and Lemoine (2020).

[17] Kepp and Bjørnskov (2021) is one such study. They use evidence from a quasi-natural experiment in the Danish region of Northern Jutland. After the discovery of mutations of Sars-CoV-2 in mink – a major Danish export – seven of the 11 municipalities of the region went into extreme lockdown in early November, while the four other municipalities retained the moderate restrictions of the remaining country. Their analysis shows that while infection levels decreased, they did so before lockdown was in effect, and infection numbers also decreased in neighbor municipalities without mandates. They conclude that efficient infection surveillance and voluntary compliance make full lockdowns unnecessary, at least in some circumstances. Kepp and Bjørnskov (2021) is not included in our review, because they focus on cases and not COVID-19 mortality. Dave et al. (2020) is another such study. They see the Wisconsin Supreme Court abolishment of Wisconsin's "Safer at Home" order (a SIPO) as a natural experiment and find that "the repeal of the state SIPO impacted social distancing, COVID-19 cases, or COVID-19-related mortality during the fortnight following enactment." Dave et al. (2020) is not included in our review, because they use a synthetic control method.

approximately 500 fewer deaths the first 11 weeks of 2020 and 4,500 fewer deaths in 2019 compared to *synthetic Sweden*.

This problem is inherent in all synthetic control studies of COVID-19, Bjørnskov argues, because the synthetic control should be fitted based on a long period of time before the intervention or the event one is studying the consequences of – i.e., the lockdown Abadie (2021). However, this is not possible for the coronavirus pandemic, as there clearly *is* no long period with coronavirus before the lockdown. Hence, the synthetic control study approach is *by design* not appropriate for studying the effect of lockdowns.

Jurisdictional variance - few observations

We exclude all interrupted time series studies which simply compare mortality rates before and after lockdowns. Simply comparing data from before and after the imposition of lockdowns could be the result of time-dependent variations, such as seasonal effects. For the same reason, we also exclude studies with little jurisdictional variance.[18] For example, we exclude Conyon et al. (2020b) who "exploit policy variation between Denmark and Norway on the one hand and Sweden on the other" and, thus, only have one jurisdictional area in the control group. Although this *is* a difference-in-difference approach, there is a non-negligible risk that differences are caused by much more than just differences in lockdowns. Another example is Wu and Wu (2020), who use all U.S. states, but pool groups of states so they end with basically three observations. None of the excluded studies cover more than 10 jurisdictional areas.[19] One study is a special case of the jurisdictional variance criteria (Auger et al. (2020). Those researchers analyze the effect of school closures in U.S. states and find that those closures reduce mortality by 35%. However, all 50 states closed schools between March 13, 2020, and March 23, 2020, which means that all difference-in-difference is based on maximum 10 days. Given the long lag between infection and death, there is a risk that Auger et al.'s approach is an interrupted time series analysis where they compare United States before and after school closures, rather than a true difference-in-difference approach. However, we choose to include this study, as it is eligible under our protocol Herby et al. (2021).

Publication status and date

We include all *ex post* studies regardless of publication status and date. That is, we cover both working papers and papers published in journals. We include the early papers because the knowledge of the COVID-19-pandemic grew rapidly in the beginning, making later papers able to stand on the shoulders of previous work. Also, in the early days of COVID-19, speed was

[18] A jurisdictional area can be countries, U.S. states, or counties. With "jurisdictional variance" we refer to variation in mandates across jurisdictional areas.

[19] All studies excluded on this criterion are listed in footnote 12.

crucial which may have affected the quality of the papers. Including them makes it possible to compare the results of early studies to studies carried out at a later stage.[20]

The role of optimal timing

We exclude papers which analyze the effect of early lockdowns in contrast to later lockdowns. There's no doubt that being prepared for a pandemic and knowing when it arrives at your doorstep is vital. However, at least two problems arise with respect to evaluating the effect of well-timed lockdowns.

First, when COVID-19 hit Europe and the United States, it was virtually impossible to determine the right timing. The World Health Organization declared the outbreak a pandemic on March 11, 2020, but at that date, Italy had already registered 13.7 COVID-19 deaths per million. On March 29, 2020, 18 days after the WHO declared the outbreak a pandemic and the earliest a lockdown response to the WHO's announcement could potentially have an effect, the mortality rate in Italy was a staggering 178 COVID-19 deaths per million with an additional 13 per million dying each day.[21]

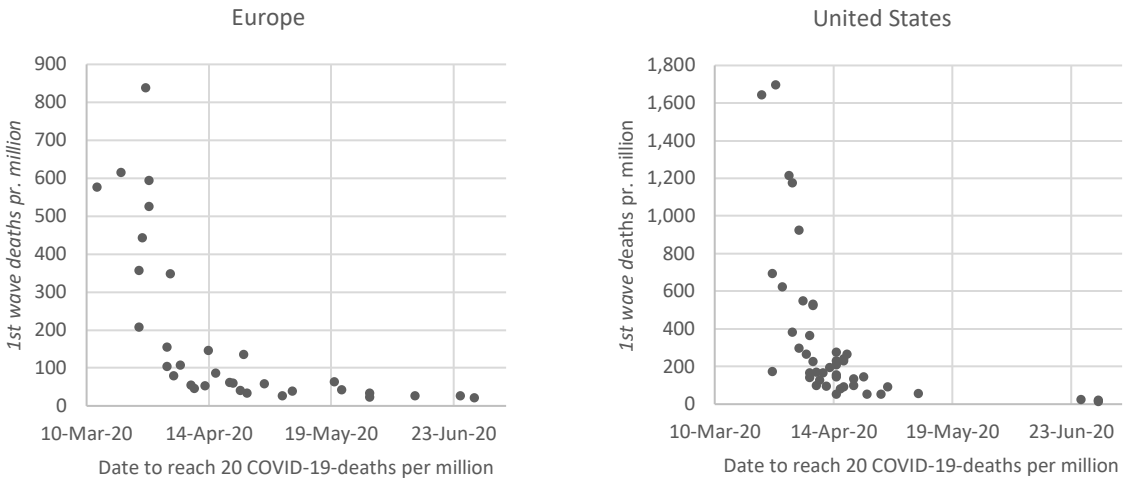
Secondly, it is extremely difficult to differentiate between the effect of public awareness and the effect of lockdowns when looking at timing because people and politicians are likely to react to the same information. As Figure 4 illustrates, all European countries and U.S. states that were hit hard and early by COVID-19 experienced high mortality rates, whereas all countries hit relatively late experienced low mortality rates. Björk et al. (2021) illustrate the difficulties in analyzing the effect of timing. They find that a 10-stringency-points-stricter lockdown would reduce COVID-19 mortality by a total of 200 deaths per million[22] if done in week 11, 2020, but would only have approximately 1/3 of the effect if implemented one week earlier or later and no effect if implemented three weeks earlier or later. One interpretation of this result is that lockdowns do not work if people either find them unnecessary and fail to obey the mandates or if people voluntarily lock themselves down. This is the argument Allen (2021) uses for the ineffectiveness of the lockdowns he identifies. If this interpretation is true, what Björk et al. (2021) find is that information and signaling is far more important than the strictness of the lockdown. There may be other interpretations, but the point is that studies focusing on timing cannot differentiate between these interpretations. However, if lockdowns have a notable effect, we should see this effect regardless of the timing, and we should identify this effect more correctly by excluding studies that exclusively analyze timing.

[20] We also intended to exclude studies which were primarily based on data from 2021 (as these studies would be heavily affected by vaccines) and studies that did not cover at least one EU-country, the United States, one U.S. U.S. state or Latin America, and where at least one country/state was not an island. However, we did not find any such studies.

[21] There's approximately a two-to-four-week gap between infection and deaths. See footnote 29.

[22] They estimate that 10-point higher stringency will reduce excess mortality by 20 "per week and million" in the 10 weeks from week 14 to week 23.

Figure 4: **Taken by surprise. The importance of having time to prepare**



Comment: The figure shows the relationship between early pandemic strength and total 1st wave of COVID-19 death toll. On the X-axis is "Days to reach 20 COVID-19-deaths per million (measured from February 15, 2020)." The Y-axis shows mortality (deaths per million) by June 30, 2020.
Source: Reported COVID-19 deaths and OxCGRT stringency for European countries and U.S. states with more than one million citizens. Data from Our World in Data.

We are aware of one meta-analysis by Stephens et al. (2020), which looks into the importance of timing. The authors find 22 studies that look at policy and timing with respect to mortality rates, however, only four were multi-country, multi-policy studies, which could possibly account for the problems described above. Stephens et al. conclude that "the timing of policy interventions across countries relative to the first Wuhan case, first national disease case, or first national death, is not found to be correlated with mortality." (See Appendix A for further discussion of the role of timing.)

3 The empirical evidence

In this section we present the empirical evidence found through our identification process. We describe the studies and their results, but also comment on the methodology and possible identification problems or biases.

3.1 Preliminary considerations

Before we turn to the eligible studies, we present some considerations that we adopted when interpreting the empirical evidence.

Empirical interpretation

While the policy conclusions contained in some studies are based on statistically significant results, many of these conclusions are ill-founded due to the tiny impact associated with said statistically significant results. For example, Ashraf (2020) states that "social distancing

measures has proved effective in controlling the spread of [a] highly contagious virus." However, their estimates show that the average lockdown in Europe and the U.S only reduced COVID-19 mortality by 2.4%.[23] Another example is Chisadza et al. (2021). The authors argue that "less stringent interventions increase the number of deaths, whereas more severe responses to the pandemic can lower fatalities." Their conclusion is based on a negative estimate for the squared term of *stringency* which results in a total negative effect on mortality rates (i.e. fewer deaths) for stringency values larger than 124. However, the stringency index is limited to values between 0 and 100 by design, so the conclusion is clearly incorrect. To avoid any such biases, we base our interpretations solely on the empirical estimates and not on the authors' own interpretation of their results.

Handling multiple models, specifications, and uncertainties

Several studies adopt a number of models to understand the effect of lockdowns. For example, Bjørnskov (2021a) estimates the effect after one, two, three, and four weeks of lockdowns. For these studies, we select the longest time horizon analyzed to obtain the estimate closest to the long-term effect of lockdowns.

Several studies also use multiple specifications including and excluding potentially relevant variables. For these studies, we choose the model which the authors regard as their main specification. Finally, some studies have multiple models which the authors regard as equally important. One interesting example is Chernozhukov et al. (2021), who estimate two models with and without national case numbers as a variable. They show that including this variable in their model alters the results substantially. The explanation could be that people responded to national conditions. For these studies, we present both estimates in Table 1, but – following Doucouliagos and Paldam (2008) – we use an average of the estimates in our meta-analysis in order to not give more weight to a study with multiple models relative to studies with just one principal model.

For studies looking at different classes of countries (e.g. rich and poor), we report both estimates in Table 1 but use the estimate for rich Western countries in our meta-analysis, where we derive common estimates for Europe and the United States.

Effects are measured "relative to Sweden in the spring of 2020"

Virtually all countries in the world implemented mandated NPIs in response to the COVID-19 pandemic. Hence, most estimates are relative to "doing the least," which in many Western countries means relative to doing as Sweden has done, especially during the first wave, when Sweden, do to constitutional constraints, implemented very few restrictions compared to other western countries (Jonung and Hanke 2020). However, some studies *do* compare the effect of doing something to the effect of doing absolutely nothing (e.g. Bonardi et al. (2020)).

The consequence is that some estimates are relative to "doing the least" while others are relative to "doing nothing." This may lead to biases if "doing the least" works as a signal (or warning)

[23] We describe how we arrive at the 2.4% in Section 4.

which alters the behavior of the public. For example, Gupta et al. (2020) find a large effect of emergency declarations, which they argue "are best viewed as an information instrument that signals to the population that the public health situation is serious and they act accordingly," on social distancing but not of other policies such as SIPOs (shelter-in-place orders). Thus, if we compare a country issuing a SIPO to a country doing nothing, we may overestimate the effect of a SIPO, because it is the sum of the signal *and* the SIPO. Instead, we should compare the country issuing the SIPO to a country "doing the least" to estimate the *marginal* effect of the SIPO.

To take an example, Bonardi et al. (2020) find relatively large effects of doing *something* but no effect of doing *more*. They find no extra effect of stricter lockdowns relative to less strict lockdowns and state that "our results point to the fact that people might adjust their behaviors quite significantly as partial measures are implemented, which might be enough to stop the spread of the virus." Hence, whether the baseline is Sweden, which implemented a ban on large gatherings early in the pandemic, or the baseline is "doing nothing" can affect the magnitude of the estimated impacts. There is no obvious right way to resolve this issue, but since estimates in most studies are relative to doing less, we report results as compared to "doing less" when available. Hence, for Bonardi et al. we state that the effect of lockdowns is zero (compared to Sweden's "doing the least").

3.2 Overview of the findings of eligible studies

Table 1 covers the 34 studies eligible for our review.[24] Out of these 34 studies, 22 were peer-reviewed and 12 were working papers. The studies analyze lockdowns during the first wave. Most of the studies (29) use data collected before September 1st, 2020 and 10 use data collected before May 1st, 2020. Only one study uses data from 2021. All studies are cross-sectional, ranging across jurisdictions. Geographically, 14 studies cover countries worldwide, four cover European countries, 13 cover the United States, two cover Europe and the United States, and one covers regions in Italy. Seven studies analyze the effect of SIPOs, 10 analyze the effect of stricter lockdowns (measured by the OxCGRT stringency index), 16 studies analyze specific NIP's independently, and one study analyzes other measures (length of lockdown).

Several studies find no statistically significant effect of lockdowns on mortality. For example, this includes Bjørnskov (2021a) and Stockenhuber (2020) who find no significant effect of stricter lockdowns (higher OxCGRT stringency index), Sears et al. (2020) and Dave et al. (2021), who find no significant effect of SIPOs, and Chaudhry et al. (2020), Aparicio and Grossbard (2021) and Guo et al. (2021) who find no significant effect of any of the analyzed NIP's, including business closures, school closures and border closures.

Other studies find a significant negative relationship between lockdowns and mortality. Fowler et al. (2021 find that SIPOs reduce COVID-19 mortality by 35%, while Chernozhukov et al.

[24] The following information can be found for each study in Table 2.

(2021) find that employee mask mandates reduces mortality by 34% and closing businesses and bars reduces mortality by 29%.

Some studies find a significant positive relationship between lockdowns and mortality. This includes Chisadza et al. (2021), who find that stricter lockdowns (higher OxCGRT stringency index) increases COVID-19 mortality by 0.01 deaths/million per stringency point and Berry et al. (2021), who find that SIPOs increase COVID-19 mortality by 1% after 14 days.

Most studies use the number of official COVID-19 deaths as the dependent variable. Only one study, Bjørnskov (2021a), looks at total excess mortality which – although is not perfect – we perceive to be the best measure, as it overcomes the measurement problems related to properly reporting COVID-19 deaths.

Several studies explicitly claim that they estimate the actual causal relationship between lockdowns and COVID-19 mortality. Some studies use instrumental variables to justify the causality associated with their analysis, while others make causality probable using anecdotal evidence.[25] But, Sebhatu et al. (2020) show that government policies are strongly driven by the policies initiated in neighboring countries rather than by the severity of the pandemic in their own countries. In short, it is not the severity of the pandemic that drives the adoption of lockdowns, but rather the propensity to copy policies initiated by neighboring countries. The Sebhatu et al. conclusion throws into doubt the notion of a causal relationship between lockdowns and COVID-19 mortality.

Table 1: Summary of eligible studies

1. Study (Author & title)	2. Measure	3. Description	4. Results	5. Comments
Alderman and Harjoto (2020); "COVID-19: U.S. shelter-in-place orders and demographic characteristics linked to cases, mortality, and recovery rates"	COVID-19 mortality	Use State-level data from the COVID-19 Tracking Project data all U.S. states, and a multivariate regression analysis to empirically investigate the impacts of the duration of shelter-in-place orders on mortality.	Find that shelter-in-place orders are - for the average duration - associated with 1% (insignificant) fewer deaths per capita.	
Aparicio and Grossbard (2021); "Are Covid Fatalities in the U.S. Higher than in the EU, and If so, Why?"	COVID-19 mortality	Their main focus is to explain the gap in COVID-19-fatalities between Europe and the United States based on COVID-deaths and other data from 85 nations/states. They include status for "social events" (ban on public gatherings, cancellation of major events and conferences), school closures, shop closures "partial lockdowns" (e.g. night curfew) and "lockdowns" (all-day curfew) 100 days after the pandemic onset in a country/state. None of these interventions have a significant effect on COVID-19 mortality. They also find no	Find no effect of "social events" (ban on public gatherings, cancellation of major events and conferences), school closures, shop closures "partial lockdowns" (e.g. night curfew) and "lockdowns" (all-day curfew) 100 days after the pandemic onset.	In the abstract the authors states that "various types of social distance measures such as school closings and lockdowns, and how soon they were implemented, help explain the U.S./EUROPE gap in cumulative deaths measured 100 days after the pandemic's onset in a state or country" although their estimates are insignificant.

[25] E.g. Dave et al. (2021) states that "estimated case reductions accelerate over time, becoming largest after 20 days following enactment of a SIPO. These findings are consistent with a causal interpretation."

1. Study (Author & title)	2. Measure	3. Description	4. Results	5. Comments
		significant effect of early cancelling of social events, school closures, shop closures, partial lockdowns and full lockdowns.		
Ashraf (2020); "Socioeconomic conditions, government interventions and health outcomes during COVID-19"	COVID-19 mortality	Their main focus is on the effectiveness of policies targeted to diminish the effect of socioeconomic inequalities (economic support) on COVID-19-deaths. They use data from 80 countries worldwide and include the OxCGRT stringency as a control variable in their models. The paper finds a significant negative (fewer deaths) effect of stricter lockdowns. The effect of lockdowns is insignificant, when they include an interaction term between the socioeconomic conditions index and the economic support index in their model.	For each 1-unit increase in OxCGRT stringency index, the cumulative mortality changes by -0.326 deaths per million (fewer deaths). The estimate is -0.073 deaths per million but insignificant, when including an interaction term between the socioeconomic conditions index and the economic support index.	
Auger et al. (2020); "Association between statewide school closure and COVID-19 incidence and mortality in the U.S."	COVID-19 mortality	U.S. population-based observational study which uses interrupted time series analyses incorporating a lag period to allow for potential policy-associated changes to occur. To isolate the association of school closure with outcomes, state-level nonpharmaceutical interventions and attributes were included in negative binomial regression models. Models were used to derive the estimated absolute differences between schools that closed and schools that remained open. The main outcome of the study is COVID-19 daily incidence and mortality per 100000 residents.	State that they adjust for several factors (e..g percentage of state's population aged 15 years and 65 years, CDC's social vulnerability index, stay-at-home or shelter-in-place order, restaurant and bar closure, testing rate per 1000 residents etc.), but does not specify how and do not present estimates.	All 50 states closed schools between March 13, 2020, and March 23, 2020. Hence, all difference-in-difference is based on maximum 10 days, and given the long lag between infection and death, there is a risk that their approach is more an interrupted time series analysis, where they compare United States before and after school closures, rather than a true difference-in-difference approach. However, we choose to include the study in our review as it - objectively speaking - lives up to the eligibility criteria specified in our protocol.
Berry et al. (2021); "Evaluating the effects of shelter-in-place policies during the COVID-19 pandemic"	COVID-19 mortality	The authors use U.S. county data on COVID-19 deaths from Johns Hopkin and SIPO data from the University of Washington to estimate the effect of SIPO's. They find no detectable effects of SIPO on deaths. The authors stress that their findings should not be interpreted as evidence that social distancing behaviors are not effective. Many people had already changed their behaviors before the introduction of shelter-in-place orders, and shelter-in-place orders appear to have been ineffective precisely because they did not meaningfully alter social distancing behavior.	SIPO increases the number of deaths by 0,654 per million after 14 days (see Fig. 2)	The authors conclude that "We do not find detectable effects of these policies [SIPO] on disease spread or deaths." However, this statement does not correspond to their results. In figure 2 they show that the effect on deaths is significant after 14 days. Looks at the effect 14 days after SIPO's are implemented which is a short lag given that the time between infection and deaths is at least 2-3 weeks.
Bjørnskov (2021a); "Did Lockdown Work? An Economist's Cross-Country Comparison"	Excess mortality	Uses excess mortality and OxCGRT stringency from 24 European countries to estimate the effect of lockdown on the number of deaths one, two, three and four weeks later. Finds no effect (negative but insignificant) of (stricter) lockdowns. The author's specification using instrument variables yields similar results.	A stricter lockdown (OxCGRT stringency) does not have a significant effect on excess mortality.	Finds a positive (more deaths) effect after one and two weeks, which could indicate that other factors (omitted variables) affect the results.
Blanco et al. (2020); "Do Coronavirus Containment Measures Work? Worldwide Evidence"	COVID-19 mortality	Use data for deaths and NPIs from Hale et al. (2020) covering 158 countries between January and August 2020 to evaluate the effect of eight different NPIs (stay at home, bans on gatherings, bans on public	When using the naïve dummy variable approach, all parameters are statistically	Run the same model four times for each of the different NPIs (stay at home-orders, ban on meetings, ban on public events and mobility restrictions). These NPIs were often introduced almost simultaneously so there is a high risk of

1. Study (Author & title)	2. Measure	3. Description	4. Results	5. Comments
		events, closing schools, lockdowns of workplaces, interruption of public transportation services, and international border closures. They address the possible endogeneity of the NPIs by using instrumental variables.	insignificant. On the contrary, estimates using the instrumental variable approach indicate that NPIs are effective in reducing the growth rate in the daily number of deaths 14 days later.	multicollinearity with each run capturing the same underlying effect. Indeed, the size and standard errors of the estimates are worryingly similar. Looks at the effect 14 days after NPIs are implemented which is a fairly short lag given the time between infection and deaths is 2-3 weeks, cf. e.g. Flaxman et al. (2020), which according to Bjørnskov (2020) appears to be the minimum typical time from infection to death).
Bonardi et al. (2020); "Fast and local: How did lockdown policies affect the spread and severity of the covid-19"	Growth rates	Use NPI data scraped from news headlines from LexisNexis and death data from Johns Hopkins University up to April 1st 2020 in a panel structure with 184 countries. Controls for country fixed effects, day fixed effects and within-country evolution of the disease.	Find that certain interventions (SIPO, regional lockdown and partial lockdown) work (in developed countries), but that stricter interventions (SIPO) do not have a larger effect than less strict interventions (e.g. restrictions on gatherings). Find no effect of border closures.	Find a positive (more deaths) effect on day 1 after lockdown which may indicate that their results are driven by other factors (omitted variables). We rely on their publicly available version submitted to CEPR Covid Economics, but estimates on the effect of deaths can be found in Supplementary material, which is available in an updated version hosted on the Danish Broadcasting Corporation's webpage: https://www.dr.dk/static/documents/2021/03/04/managing_pandemics_e3911c11.pdf
Bongaerts et al. (2021); "Closed for business: The mortality impact of business closures during the Covid-19 pandemic"	COVID-19 mortality	Uses variation in exposure to closed sectors (e.g. tourism) in municipalities within Italy to estimate the effect of business closures. Assuming that municipalities with different exposures to closed sectors are not inherently different, they find that municipalities with higher exposure to closed sectors experienced subsequently lower mortality rates.	Business shutdown saved 9,439 Italian lives by April 13th 2020. This corresponds to a reduction of deaths by 32%, as there were 20,465 COVID-19-deaths in Italy by mid April 2020.	They (implicitly) assume that municipalities with different exposures to closed sectors are not inherently different. This assumption could be problematic, as more touristed municipalities can be very different from e.g. more industrialized municipalities.
Chaudhry et al. (2020); "A country level analysis measuring the impact of government actions, country preparedness and socioeconomic factors on COVID-19 mortality and related health outcomes"	COVID-19 mortality	Uses information on COVID-19 related national policies and health outcomes from the top 50 countries ranked by number of cases. Finds no significant effect of any NPI on the number of COVID-19-deaths.	Finds no significant effect on mortality of any of the analyzed interventions (partial border closure, complete border closure, partial lockdown (physical distancing measures only), complete lockdown (enhanced containment measures including suspension of all non-essential services), and curfews).	
Chernozhukov et al. (2021); "Causal impact of masks, policies, behavior on early covid-19 pandemic in the U.S."	Growth rates	Uses COVID-deaths from the New York Times and Johns Hopkins and data for U.S. States from Raifman et al. (2020) to estimate the effect of SIPO, closed nonessential businesses, closed K-12 schools, closed restaurants except takeout, closed movie theaters, and face mask mandates for employees in public facing businesses.	Finds that mandatory masks for employees and closing K-12 schools reduces deaths. SIPO and closing business (average of closed businesses, restaurants and movie theaters) has no statistically significant effect. The effect of school closures is highly sensitive to the	States that ”our regression specification for case and death growths is explicitly guided by a SIR model although our causal approach does not hinge on the validity of a SIR model.” We are uncertain if this means that data are managed to fit an SIR-model (and thus should fail our eligibility criteria).

1. Study (Author & title)	2. Measure	3. Description	4. Results	5. Comments
			inclusion of national case and death data.	
Chisadza et al. (2021); "Government Effectiveness and the COVID-19 Pandemic"	COVID-19 mortality	Uses COVID-19-deaths and OxCGRT stringency from 144 countries to estimate the effect of lockdown on the number of COVID-19-deaths. Find a significant positive (more deaths) non-linear association between government response indices and the number of deaths.	An increase by 1 on "stringency index" increases the number of deaths by 0.0130 per million. The sign of the squared term is negative, but the combined non-linear estimate is positive (increases deaths) and larger than the linear estimate for all values of the OxCGRT stringency index.	The author states that "less stringent interventions increase the number of deaths, whereas more severe responses to the pandemic can lower fatalities." However, according to their estimates this is not correct, as the combined non-linear estimate cannot be negative for relevant values of the OxCGRT stringency index (0 to 100).
Dave et al. (2021); "When Do Shelter-in-Place Orders Fight Covid-19 Best? Policy Heterogeneity Across States and Adoption Time"	COVID-19 mortality	Uses smartphone location tracking and state data on COVID-19 deaths and SIPO data (supplemented by their own searches) collected by the New York Times to estimate the effect of SIPO's. Finds that SIPO was associated with a 9%–10% increase in the rate at which state residents remained in their homes full-time, but overall they do not find an significant effect on mortality after 20+ days (see Figure 4). Indicate that the lacking significance may be due to long term estimates being identified of a few early adopting states.	Finds no overall significant effect of SIPO on deaths but does find a negative effect (fewer deaths) in early adopting states.	Find large effects of SIPO on deaths after 6-14 days in early adopting states (see Table 8), which is before an SIPO-related effect would be seen. This could indicate that other factors rather than SIPO's drive the results.
Dergiades et al. (2020); "Effectiveness of government policies in response to the COVID-19 outbreak"	COVID-19 mortality	Uses daily deaths from the European Centre for Disease Prevention and Control and OxCGRT stringency from 32 countries worldwide (including U.S.) to estimates the effect of lockdown on the number of deaths.	Finds that the greater the strength of government interventions at an early stage, the more effective these are in slowing down or reversing the growth rate of deaths.	Focus is on the effect of early stage NPIs and thus does not absolutely live up to our eligibility criteria. However, we include the study as it differentiates between lockdown strength at an early stage.
Fakir and Bharati (2021); "Pandemic catch-22: The role of mobility restrictions and institutional inequalities in halting the spread of COVID-19"	COVID-19 mortality	Uses data from 127 countries. combining high-frequency measures of mobility data from Google's daily mobility reports, country-date-level information on the stringency of restrictions in response to the pandemic from Oxford's Coronavirus Government Response Tracker (OxCGRT), and daily data on deaths attributed to COVID-19 from Our World In Data and the Johns Hopkins University. Instrument stringency using day-to-day changes in the stringency of the restrictions in the rest of the world.	Find large causal effects of stricter restrictions on the weekly growth rate of recorded deaths attributed to COVID-19. Show that more stringent interventions help more in richer, more educated, more democratic, and less corrupt countries with older, healthier populations and more effective governments.	Finds a larger effect on deaths after 0 days than after 14 and 21 days (Table 3). This is surprising given that it takes 2-3 weeks from infection to death, and it may indicate that their results are driven by other factors.
Fowler et al. (2021); "Stay-at-home orders associate with subsequent decreases in COVID-19 cases and fatalities in the United States"	COVID-19 mortality	Uses U.S. county data on COVID-19 deaths and SIPO data collected by the New York Times to estimate the effect of SIPO's using a two-way fixed-effects difference-in-differences model. Find a large and early (after few days) effect of SIPO on COVID-19 related deaths.	Stay-at-home orders are also associated with a 59.8 percent (18.3 to 80.2) average reduction in weekly fatalities after three weeks. These results suggest that stay-at-home orders	Finds the largest effect of SIPO on deaths after 10 days (see Figure 4), before a SIPO-related effect could possibly be seen as it takes 2-3 weeks from infection to death. This could indicate that other factors drive their results.

1. Study (Author & title)	2. Measure	3. Description	4. Results	5. Comments
			might have reduced confirmed cases by 390,000 (170,000 to 680,000) and fatalities by 41,000 (27,000 to 59,000) within the first three weeks in localities that implemented stay-at-home orders.	
Fuller et al. (2021); "Mitigation Policies and COVID-19–Associated Mortality — 37 European Countries, January 23–June 30, 2020"	COVID-19 mortality	Uses COVID-19-deaths and OxCGRT stringency in 37 European countries to estimate the effect of lockdown on the number of COVID-19-deaths. Find a significant negative (fewer deaths) effect of stricter lockdowns after mortality threshold is reached (the threshold is a daily rate of 0.02 new COVID-19 deaths per 100,000 population (based on a 7-day moving average))	For each 1-unit increase in OxCGRT stringency index, the cumulative mortality decreases by 0.55 deaths per 100,000.	
Gibson (2020); "Government mandated lockdowns do not reduce Covid-19 deaths: implications for evaluating the stringent New Zealand response"	COVID-19 mortality	Uses data for every county in the United States from March through June 1, 2020, to estimate the effect of SIPO (called "lockdown") on COVID-19 mortality. Policy data are acquired from American Red Cross reporting on emergency regulations. His control variables include county population and density, the elder share, the share in nursing homes, nine other demographic and economic characteristics and a set of regional fixed effects. Handles causality problems using instrument variables (IV).	Find no statistically significant effect of SIPO.	Gibson use the word "lockdown" as synonym for SIPO (writes "technically, government-ordered community quarantine")
Goldstein et al. (2021); "Lockdown Fatigue: The Diminishing Effects of Quarantines on the Spread of COVID-19 "	COVID-19 mortality	Uses panel data from 152 countries with data from the onset of the pandemic until December 31, 2020. Finds that lockdowns tend to reduce the number of COVID-19 related deaths, but also that this benign impact declines over time: after four months of strict lockdown, NPIs have a significantly weaker contribution in terms of their effect in reducing COVID-19 related fatalities.	Stricter lockdowns reduce deaths for the first 60 days, whereafter the cumulative effect begins to decrease. If reintroduced after 120, the effect of lockdowns is smaller in the short run, but after 90 days the effect is almost the same as during first lockdown (only app. 10% lower).	There is little documentation in the study (e.g. no tables with estimates).
Guo et al. (2021); "Mitigation Interventions in the United States: An Exploratory Investigation of Determinants and Impacts"	COVID-19 mortality	Uses policy data from 1,470 executive orders from the state–government websites for all 50 states and Washington DC and COVID-19-deaths from Johns Hopkins University in a random-effect spatial error panel model to estimate the effect of nine NPIs (SIPO, strengthened SIPO, public school closure, all school closure, large-gathering ban of more than 10 people, any gathering ban, restaurant/bar limit to dining out only, nonessential business closure, and mandatory self-quarantine of travelers) on COVID-19 deaths.	Two mitigation strategies (all school closure and mandatory self-quarantine of travelers) showed positive (more deaths) impact on COVID-19-deaths per 10,000. Six mitigation strategies (SIPO, public school closure, large gathering bans (>10), any gathering ban, restaurant/bar limit to dining out only, and nonessential business	Only conclude on NPIs which reduce mortality. However, the conclusion is based on one-tailed tests, which means that all positive estimates (more deaths) are deemed insignificant. Thus, in their mortality-specification (Table 3, Proportion of Cumulative Deaths Over the Population), the estimate of all school closures (.204) and mandatory self-quarantine of travelers (0.363) is deemed insignificant based on schools CI [.029, .379] and quarantine CI [.193, .532]. We believe, these results should be interpreted as a significant increase in mortality, and that these results should have been part of their conclusion.

1. Study (Author & title)	2. Measure	3. Description	4. Results	5. Comments
			closure) did not show any impact (Table 3, "Proportion of Cumulative Deaths Over the Population).	
Hale et al. (2020); "Global assessment of the relationship between government response measures and COVID-19 deaths"	COVID-19 mortality	Uses the OxCGRT stringency and COVID-19-deaths from the European Centre for Disease Prevention and Control for 170 countries. Estimates both cross-sectional models in which countries are the unit of analysis, as well as longitudinal models on time-series panel data with country-day as the unit of analysis (including models that use both time and country fixed effects).	Finds that higher stringency in the past leads to a lower growth rate in the present, with each additional point of stringency corresponding to a 0.039%-point reduction in daily deaths growth rates six weeks later.	
Hunter et al. (2021); "Impact of non-pharmaceutical interventions against COVID-19 in Europe: A quasi-experimental non-equivalent group and time-series"	COVID-19 mortality	Uses death data from the European Centre for Disease Prevention and Control (ECDC) and NPI-data from the Institute of Health Metrics and Evaluation. Argues that they use a quasi-experimental approach to identify the effect of NPIs because no analyzed intervention was imposed by all European countries and interventions were put in place at different points in the development of the epidemics.	Finds that mass gathering restrictions and initial business closures (businesses such as entertainment venues, bars and restaurants) reduces the number of deaths, whereas closing educational facilities and issuing SIPO increases the number of deaths. Finds no effect of closing non-essential services and mandating/recommending masks (Table 3)	Finds an effect of closing educational facilities and non-essential services after 1-7 days before lockdown could possibly have an effect on the number of deaths. This may indicate that other factors are driving their results.
Langeland et al. (2021); "The Effect of State Level COVID-19 Stay-at-Home Orders on Death Rates"	COVID-19 mortality	Estimates the effect of state-level lockdowns on COVID-19 deaths using multiple quasi-Poisson regressions with lockdown time length as the explanatory variable. Does not specify how lockdown is defined and what their data sources are.	Finds no significant effect of SIPO on the number of deaths after 2-4, 4-6 and 6+ weeks.	They write that "6+ weeks of lockdown is the only setting where the odds of dying are statistically higher than in the no lockdown case." However, all estimates are insignificant in Table C. Looks as if lockdown duration may cause a causality problem, because politicians may be less likely to ease restrictions when there are many cases/deaths.
Leffler et al. (2020); "Association of country-wide coronavirus mortality with demographics, testing, lockdowns, and public wearing of masks"	COVID-19 mortality	Use COVID-19 deaths from Worldometer and info about NPIs (mask/mask recommendations, international travel restrictions and lockdowns (defined as any closure of schools or workplaces, limits on public gatherings or internal movement, or stay-at-home orders) from Hale et al. (2020) for 200 countries to estimate the effect of the duration of NPIs on the number of deaths.	Finds that masking (mask recommendations) reduces mortality. For each week that masks were recommended the increase in per-capita mortality was 8.1% (compared to 55.7% increase when masks were not recommended). Finds no significant effect of the number of weeks with internal lockdowns and international travel restrictions (Table 2).	Their "mask recommendation" category includes some countries, where masks were mandated (see Supplemental Table A1) and may (partially) capture the effect of mask mandates. Looks at duration which may cause a causality problem, because politicians may be less likely to ease restrictions when there are many cases/deaths.
Mccafferty and Ashley (2021); "Covid-19 Social Distancing Interventions by Statutory Mandate and Their Observational	Other	Use data from 27 U.S. states and 12 European countries to analyze the effect of NPIs on peak morality rate using general linear mixed effects modelling.	Finds that no mandate (school closures, prohibition on mass gatherings, business closures, stay at home	

1. Study (Author & title)	2. Measure	3. Description	4. Results	5. Comments
Correlation to Mortality in the United States and Europe"			orders, severe travel restrictions, and closure of non-essential businesses) was effective in reducing the peak COVID-19 mortality rate.	
Pan et al. (2020); "Covid-19: Effectiveness of non-pharmaceutical interventions in the united states before phased removal of social distancing protections varies by region"	COVID-19 mortality	Uses county-level data for all U.S. states. Mortality is obtained from Johns Hopkins, while policy data are obtained from official governmental websites. Categorizes 12 policies into 4 levels of disease control; Level 1 (low) - State of Emergency; Level 2 (moderate) - school closures, restricting access (visits) to nursing homes, or closing restaurants and bars; Level 3 (high) - non-essential business closures, suspending non-violent arrests, suspending elective medical procedures, suspending evictions, or restricting mass gatherings of at least 10 people; and Level 4 (aggressive) - sheltering in place / stay-at-home, public mask requirements, or travel restrictions. Use stepped-wedge cluster randomized trial (SW-CRT) for clustering and negative binomial mixed model regression.	Concludes that only (duration of, see comment in next column) level 4 restrictions are associated with reduced risk of death, with an average 15% decline in the COVID-19 death rate per day. Implementation of level 3 and level 2 restrictions increased death rates in 6 of 6 regions, while longer duration increased death rates in 5 of 6 regions.	They focus on the negative estimate of duration of Level 4. However, their implementation estimate is large and positive, and the combined effect of implementation and duration is unclear.
Pincombe et al. (2021); "The effectiveness of national-level containment and closure policies across income levels during the COVID-19 pandemic: an analysis of 113 countries"	COVID-19 mortality	Uses daily data for 113 countries on cumulative COVID-19 death counts over 130 days between February 15, 2020, and June 23, 2020, to examine changes in mortality growth rates across the World Bank's income group classifications following shelter-in-place recommendations or orders (they use one variable covering both recommendations and orders).	Finds that shelter-in-place recommendations/orders reduces mortality growth rates in high income countries (although insignificant) but increases growth rates in countries in other income groups.	
Sears et al. (2020); "Are we #stayinghome to Flatten the Curve?"	COVID-19 mortality	Uses cellular location data from all 50 states and the District of Columbia to investigate mobility patterns during the pandemic across states and time. Adding COVID-19 death tolls and the timing of SIPO for each state they estimate the effect of stay-at-home policies on COVID-19 mortality.	Find that SIPOs lower deaths by 0.13- 0.17 per 100,000 residents, equivalent to death rates 29-35% lower than in the absence of policies. However, these estimates are insignificant at a 95% confidence interval (see Table 4). The study also finds reductions in activity levels prior to mandates. Human encounter rate fell by 63 percentage points and nonessential visits by 39 percentage points relative to pre-COVID-19 levels, prior to any state implementing a statewide mandate	In the abstract the authors state that death rates would be 42-54% lower than in the absence of policies. However, this includes averted deaths due to pre-mandate social distancing behavior (p. 6). The effect of SIPO is a reduction in deaths by 29%-35% compared to a situation without SIPO but with pre-mandate social distancing. These estimates are insignificant at a 95% confidence interval.

1. Study (Author & title)	2. Measure	3. Description	4. Results	5. Comments
Shiva and Molana (2021); "The Luxury of Lockdown"	COVID-19 mortality	Uses COVID-19-deaths and OxCGRT stringency from 169 countries to estimate the effect of lockdown on the number of deaths 1-8 weeks later. Finds that stricter lockdowns reduce COVID-19-deaths 4 weeks later (but insignificant 8 weeks later) and have the greatest effect in high income countries. Finds no effect of workplace closures in low-income countries.	A stricter lockdown (1 stringency point) reduces deaths by 0,1% after 4 weeks. After 8 weeks the effect is insignificant.	
Spiegel and Tookes (2021); "Business restrictions and Covid-19 fatalities"	COVID-19 mortality	Use data for every county in the United States from March through December 2020 to estimate the effect of various NPIs on the COVID-19-deaths growth rate. Derives causality by 1) assuming that state regulators primarily focus on the state's most populous counties, so state regulation in smaller counties can be viewed as a quasi randomized experiment, and 2) conducting county pair analysis, where similar counties in different states (and subject to different state policies) are compared.	Finds that some interventions (e.g. mask mandates, restaurant and bar closures, gym closures, and high-risk business closures) reduces mortality growth, while other interventions (closures of low- to medium-risk businesses and personal care/spa services) did not have an effect and may even have increased the number of deaths.	In total they analyze the lockdown effect of 21 variables. 14 of 21 estimates are significant, and of these 6 are negative (reduces deaths) while 8 are positive (increases deaths). Some results are far from intuitive. E.g. mask recommendations increases deaths by 48% while mask mandates reduces deaths by 12%, and closing restaurants and bars reduces deaths by 50%, while closing bars but not restaurants only reduces deaths by 5%.
Stockenhuber (2020); "Did We Respond Quickly Enough? How Policy-Implementation Speed in Response to COVID-19 Affects the Number of Fatal Cases in Europe"	COVID-19 mortality	Uses data for the number of COVID-19 infections and deaths and policy information for 24 countries from OxCGRT to estimate the effect of stricter lockdowns on the number of deaths using principal component analysis and a generalized linear mixed model.	Finds no significant effect of stricter lockdowns on the number of fatalities (Table 4).	Groups data on lockdown strictness into four groups and lose significant information and variation.
Stokes et al. (2020); "The relative effects of non-pharmaceutical interventions on early Covid-19 mortality: natural experiment in 130 countries"	COVID-19 mortality	Uses daily Covid-19 deaths for 130 countries from the European Centre for Disease Prevention and Control (ECDC) and daily policy data from the Oxford COVID-19 Government Response Tracker (OxCGRT). Looks at all levels of restrictions for each of the nine sub-categories of the OxCGRT stringency index (school, work, events, gatherings, transport, SIPO, internal movement, travel).	Of the nine sub-categories in the OxCGRT stringency index, only travel restrictions are consistently significant (with level 2 "Quarantine arrivals from high-risk regions" having the largest effect, and the strictest level 4 "Total border closure" having the smallest effect). Restrictions on very large gatherings (>1,000) has a large significant negative (fewer deaths) effect, while the effect of stricter restrictions on gatherings are insignificant. Authors recommend that the closing of schools (level 1) has a very large (in absolute terms it's twice the effect of border quarantines) positive	Their results are counter intuitive and somewhat inconclusive. Why does limiting very large gatherings (>1,000) work, while stricter limits do not? Why do recommending school closures cause more deaths? Why is the effect of border closures before 1st death insignificant, while the effect of closing borders after 1st death is significant (and large)? And why does quarantining arrivals from high-risk regions work better than total border closures? With 23 estimated parameters in total these counter intuitive and inconclusive results could be caused by multiple test bias (we correct for this in the meta-analysis), but may also be caused by other factors such as omitted variable bias.

1. Study (Author & title)	2. Measure	3. Description	4. Results	5. Comments
			effect (more deaths) while stricter interventions on schools have no significant effect. Required cancelling of public events also has a significant positive (more deaths) effect. We focus on their 14-38 days results, as they catch the longest time frame (their 0-24 day model returns mostly insignificant results).	
Toya and Skidmore (2020); "A Cross-Country Analysis of the Determinants of Covid-19 Fatalities"	COVID-19 mortality	Uses COVID-19-deaths and lockdown info from various sources from 159 countries in a cross-country event study. Controls for country specifics by including socio-economic, political, geographic, and policy information. Finds little evidence for the efficacy of NPIs.	Complete travel restrictions prior to April 2020 reduced deaths by -0.226 per 100.000 by April 1st 2021, while mandatory national lockdown prior to April 2020 increased deaths by 0.166 by April 1st 2021. Recommended local lockdowns reduced deaths but results are based on one observation. Partial travel restrictions, mandatory local lockdowns and recommended national lockdowns did not have a significant effect on deaths.	The study looks at the lockdown status prior to April 2020 and the effect on deaths the following year (until April 1st 2021). The authors state this is to reduce concerns about endogeneity but do not explain why the lockdowns in the spring of 2020 are a good instrument for lockdowns during later waves are.
Tsai et al. (2021); "Coronavirus Disease 2019 (COVID-19) Transmission in the United States Before Versus After Relaxation of Statewide Social Distancing Measures"	Reproduction rate, Rt	Uses data for NPIs that were implemented and/or relaxed in U.S. states between 10 March and 15 July 2020. Using segmented linear regression, they estimate the extent to which relaxation of social distancing affected epidemic control, as indicated by the time-varying, state-specific effective reproduction number (Rt). Rt is based on death tolls.	Finds that in the 8 weeks prior to relaxing NPIs, Rt was declining, while after relaxation Rt started to increase.	Their Figure 1 shows that Rt on average increases app. 10 days before relaxation, which could indicate that other factors (omitted variables) affect the results.

Note: All comments on the significance of estimates are based on a 5% significance level unless otherwise stated.

It is difficult to make a conclusion based on the overview in Table 1. Is -0.073 to -0.326 deaths/million per stringency point, as estimated by Ashraf (2020), a large or a small effect relative to. the 98% reduction in mortality predicted by the study published by the Imperial College London (Ferguson et al. (2020). This is the subject for our meta-analysis in the next section. Here, it turns out that -0.073 to -0.326 deaths/million per stringency point is a relatively modest effect and only corresponds to a 2.4% reduction in COVID-19 mortality on average in the U.S. and Europe.

4 Meta-analysis: The impact of lockdowns on COVID-19 mortality

We now turn to the meta-analysis, where we focus on the impact of lockdowns on COVID-19 mortality.

In the meta-analysis, we include 24 studies in which we can derive the relative effect of lockdowns on COVID-19 mortality, where mortality is measured as COVID-19-related deaths per million. In practice, this means that the studies we included estimate the effect of lockdowns on mortality or the effect of lockdowns on mortality growth rates, while using a counterfactual estimate.[26]

Our focus is on the effect of compulsory non-pharmaceutical interventions (NPI), policies that restrict internal movement, close schools and businesses, and ban international travel, among others. We do not look at the effect of voluntary behavioral changes (e.g. voluntary mask wearing), the effect of recommendations (e.g. recommended mask wearing), or governmental services (voluntary mass testing and public information campaigns), but only on mandated NPIs.

The studies we examine are placed in three categories. Seven studies analyze the effect of stricter lockdowns based on the OxCGRT stringency indices, 13 studies analyze the effect of SIPOs (6 studies only analyze SIPOs, while seven analyze SIPOs among other interventions), and 11 studies analyze the effect of specific NPIs independently (lockdown vs. no lockdown).[27] Each of these categories is handled so that comparable estimates can be made across categories. Below, we present the results for each category and show the overall results, as well as those based on various quality dimensions.

Quality dimensions

We include quality dimensions because there are reasons to believe that can affect a study's conclusion. Below we describe the dimensions, as well as our reasons to believe that they are necessary to fully understand the empirical evidence.

- *Peer-reviewed vs. working papers*: We distinguish between peer-reviewed studies and working papers as we consider peer-reviewed studies generally being of higher quality than working papers.[28]

- *Long vs. short time period*: We distinguish between studies based on long time periods (with data series ending *after* May 31, 2020) and short time periods (data series ending at or before May 31, 2020), because the first wave did not fully end before late June in the U.S. and Europe. Thus, studies relying on short data periods lack the last part of the first wave and may yield biased results if lockdowns only "flatten the curve" and do not prevent deaths.

[26] As a minimum requirement, one needs to know the effect on the top of the curve.
[27] The total is larger than 21 because the 11 SIPO studies include seven studies which look at multiple measures.
[28] Vetted papers from CEPR Covid Economics are considered as working papers in this regard.

- *No early effect on mortality*: On average, it takes approximately three weeks from infection to death.[29] However, several studies find effects of lockdown on mortality almost immediately. Fowler et al. (2021) find a significant effect of SIPOs on mortality after just four days and the largest effect after 10 days. An early effect may indicate that other factors (omitted variables) drive the results, and, thus, we distinguish between studies which find an effect on mortality sooner than 14 days after lockdown and those that do not.[30] Note that many studies do not look at the short term and thus fall into the latter category by default.

- *Social sciences vs. other sciences*: While it is true that epidemiologists and researchers in natural sciences should, in principle, know much more about COVID-19 and how it spreads than social scientists, social scientists are, in principle, experts in evaluating the effect of various policy interventions. Thus, we distinguish between studies published by scholars in social sciences and by scholars from other fields of research. We perceive the former as being better suited for examining the effects of lockdowns on mortality. For each study, we have registered the research field for the corresponding author's associated institute (e.g., for a scholar from "Institute of economics" research field is registered as "Economics"). Where no corresponding author was available, the first author has been used. Afterwards, all research fields have been classified as either from the "Social Science" or "Other.""[31]

We also considered including a quality dimension to distinguish between studies based on excess mortality and studies based on COVID-19 mortality, as we believe that excess mortality is potentially a better measure for two reasons. First, data on total deaths in a country is far more precise than data on COVID-19 related deaths, which may be both underreported (due to lack of tests) or overreported (because some people die *with* – but not *because of* – COVID-19). Secondly, a major purpose of lockdowns is to save lives. To the extend lockdowns shift deaths *from* COVID-19 *to* other causes (e.g. suicide), estimates based on COVID-19 mortality will overestimate the effect of lockdowns. Likewise, if lockdowns save lives in other ways (e.g. fewer traffic accidents) lockdowns' effect on mortality will be underestimated. However, as only one

[29] Leffler et al. (2020) writes, "On average, the time from infection with the coronavirus to onset of symptoms is 5.1 days, and the time from symptom onset to death is on average 17.8 days. Therefore, the time from infection to death is expected to be 23 days." Meanwhile, Stokes et al. (2020) writes that "evidence suggests a mean lag between virus transmission and symptom onset of 6 days, and a further mean lag of 18 days between onset of symptoms and death."

[30] Some of the authors are aware of this problem. E.g. Bjørnskov (2021a) writes "when the lag length extends to three or fourth weeks, that is, the length that is reasonable from the perspective of the virology of Sars-CoV-2, the estimates become very small and insignificant" and "these results confirm the overall pattern by being negative and significant when lagged one or two weeks (the period when they cannot have worked) but turning positive and insignificant when lagged four weeks."

[31] Research fields classified as social sciences were economics, public health, management, political science, government, international development, and public policy, while research fields not classified as social sciences were ophthalmology, environment, medicine, evolutionary biology and environment, human toxicology, epidemiology, and anesthesiology.

of the 34 studies (Bjørnskov (2021a)) is based on excess mortality, we are unfortunately forced to disregard this quality dimension.

Meta-data used for our quality dimensions as well as other relevant information are shown in Table 2.

Table 2: Metadata for the studies included in the meta-analysis

1. Study (Author & title)	2. Included in meta-analysis	3. Publication status	4. End of data period	5. Earliest effect	6. Field of research	7. Lockdown measure	8. Geographical coverage
Alderman and Harjoto (2020); "COVID-19: U.S. shelter-in-place orders and demographic characteristics linked to cases, mortality, and recovery rates"	Yes	Peer-review	11-Jun-20	n/a	Economics (Social science)	SIPO	United States
Aparicio and Grossbard (2021); "Are Covid Fatalities in the U.S. Higher than in the EU, and If so, Why?"	Yes	Peer-review	22-Jul-20	n/a	Economics (Social science)	Specific NPIs	Europe and United States
Ashraf (2020); "Socioeconomic conditions, government interventions and health outcomes during COVID-19"	Yes	WP	20-May-20	n/a	Economics (Social science)	Stringency	World
Auger et al. (2020); "Association between statewide school closure and COVID-19 incidence and mortality in the U.S."	Yes	Peer-review	07-May-20	>21 days	Medicine (Other)	Specific NPIs	United States
Berry et al. (2021); "Evaluating the effects of shelter-in-place policies during the COVID-19 pandemic"	Yes	Peer-review	30-May-20	8-14 days	Public policy (Social science)	SIPO	United States
Bjørnskov (2021a); "Did Lockdown Work? An Economist's Cross-Country Comparison"	Yes	Peer-review	30-Jun-20	<8 days	Economics (Social science)	Stringency	Europe
Blanco et al. (2020); "Do Coronavirus Containment Measures Work? Worldwide Evidence"	No	WP	31-Aug-20	8-14 days	Economics (Social science)	Specific NPIs	World
Bonardi et al. (2020); "Fast and local: How did lockdown policies affect the spread and severity of the covid-19"	Yes	WP	13-Apr-20	<8 days	Economics (Social science)	Specific NPIs	World
Bongaerts et al. (2021); "Closed for business: The mortality impact of business closures during the Covid-19 pandemic"	Yes	Peer-review	13-Apr-20	8-14 days	Management (Social science)	Specific NPIs	One country
Chaudhry et al. (2020); "A country level analysis measuring the impact of government actions, country preparedness and socioeconomic factors on COVID-19 mortality and related health outcomes"	Yes	Peer-review	01-Apr-20	n/a	Anesthesiology (Other)	Specific NPIs	World
Chernozhukov et al. (2021); "Causal impact of masks, policies, behavior on early covid-19 pandemic in the U.S."	Yes	Peer-review	03-Aun-20	n/a	Economics (Social science)	Specific NPIs	United States
Chisadza et al. (2021); "Government Effectiveness and the COVID-19 Pandemic"	Yes	Peer-review	01-Sep-20	n/a	Economics (Social science)	Stringency	World
Dave et al. (2021); "When Do Shelter-in-Place Orders Fight Covid-19 Best? Policy Heterogeneity Across States and Adoption Time"	Yes	Peer-review	20-Apr-20	Finds no effect	Economics (Social science)	SIPO	United States
Dergiades et al. (2020); "Effectiveness of government policies in response to the COVID-19 outbreak"	No	WP	30-Apr-20	n/a	Management (Social science)	Stringency	World
Fakir and Bharati (2021); "Pandemic catch-22: The role of mobility restrictions and institutional inequalities in halting the spread of COVID-19"	No	Peer-review	30-Jul-20	<8 days	Economics (Social science)	Stringency	World

1. Study (Author & title)	2. Included in meta-analysis	3. Publication status	4. End of data period	5. Earliest effect	6. Field of research	7. Lockdown measure	8. Geographical coverage
Fowler et al. (2021); "Stay-at-home orders associate with subsequent decreases in COVID-19 cases and fatalities in the United States"	Yes	Peer-review	07-May-20	<8 days	Public Health (Social science)	SIPO	United States
Fuller et al. (2021); "Mitigation Policies and COVID-19–Associated Mortality — 37 European Countries, January 23–June 30, 2020"	Yes	WP	30-Jun-20	n/a	Epidemiology (Other)	Stringency	Europe
Gibson (2020); "Government mandated lockdowns do not reduce Covid-19 deaths: implications for evaluating the stringent New Zealand response"	Yes	Peer-review	01-Jun-20	Finds no effect	Economics (Social science)	SIPO	United States
Goldstein et al. (2021); "Lockdown Fatigue: The Diminishing Effects of Quarantines on the Spread of COVID-19 "	Yes	WP	31-Dec-20	<8 days	International Development (Social science)	Stringency	World
Guo et al. (2021); "Mitigation Interventions in the United States: An Exploratory Investigation of Determinants and Impacts"	Yes	Peer-review	07-Apr-20	n/a	Social work (Social science)	Specific NPIs	United States
Hale et al. (2020); "Global assessment of the relationship between government response measures and COVID-19 deaths"	No	WP	27-May-20	n/a	Government (Social science)	Stringency	World
Hunter et al. (2021); "Impact of non-pharmaceutical interventions against COVID-19 in Europe: A quasi-experimental non-equivalent group and time-series"	No	Peer-review	24-Apr-20	<8 days	Medicine (Other)	Specific NPIs	Europe
Langeland et al. (2021); "The Effect of State Level COVID-19 Stay-at-Home Orders on Death Rates"	No	WP	Not specified	Finds no effect	Political Science (Social science)	Other	United States
Leffler et al. (2020); "Association of country-wide coronavirus mortality with demographics, testing, lockdowns, and public wearing of masks"	Yes	Peer-review	09-May-20	n/a	Ophthalmology (Other)	Specific NPIs	World
Mccafferty and Ashley (2021); "Covid-19 Social Distancing Interventions by Statutory Mandate and Their Observational Correlation to Mortality in the United States and Europe"	No	Peer-review	12-Apr-20	Finds no effect	Ophthalmology (Other)	Specific NPIs	Europe and United States
Pan et al. (2020); "Covid-19: Effectiveness of non-pharmaceutical interventions in the united states before phased removal of social distancing protections varies by region"	No	WP	29-May-20	n/a	Environment (Other)	Specific NPIs	United States
Pincombe et al. (2021); "The effectiveness of national-level containment and closure policies across income levels during the COVID-19 pandemic: an analysis of 113 countries"	No	Peer-review	23-Jun-20	n/a	Health Science (Social science)	SIPO	World
Sears et al. (2020); "Are we #stayinghome to Flatten the Curve?"	Yes	WP	29-Apr-20	Finds no effect	Economics (Social science)	SIPO	United States
Shiva and Molana (2021); "The Luxury of Lockdown"	Yes	Peer-review	08-Jun-20	15-21 days	Government (Social science)	Stringency	World
Spiegel and Tookes (2021); "Business restrictions and Covid-19 fatalities"	Yes	Peer-review	31-Dec-20	<8 days	Management (Social science)	Specific NPIs	United States
Stockenhuber (2020); "Did We Respond Quickly Enough? How Policy-Implementation Speed in Response to COVID-19 Affects the Number of Fatal Cases in Europe"	Yes	Peer-review	12-Jul-20	n/a	Evolutionary Biology and Environment (Other)	Stringency	Europe
Stokes et al. (2020); "The relative effects of non-pharmaceutical interventions on early	Yes	WP	01-Jun-20	n/a	Economics (Social science)	Specific NPIs	World

1. Study (Author & title)	2. Included in meta-analysis	3. Publication status	4. End of data period	5. Earliest effect	6. Field of research	7. Lockdown measure	8. Geographical coverage
Covid-19 mortality: natural experiment in 130 countries"							
Toya and Skidmore (2020); "A Cross-Country Analysis of the Determinants of Covid-19 Fatalities"	Yes	WP	01-Apr-21	n/a	Economics (Social science)	Specific NPIs	World
Tsai et al. (2021); "Coronavirus Disease 2019 (COVID-19) Transmission in the United States Before Versus After Relaxation of Statewide Social Distancing Measures"	No	Peer-review	15-Jul-20	<8 days	Psychiatry (Social science)	Specific NPIs	United States

Note: Research fields classified as social sciences were economics, public health, health science, management, political science, government, international development, and public policy, while research fields not classified as social sciences were ophthalmology, environment, medicine, evolutionary biology and environment, human toxicology, epidemiology and anesthesiology.

Interpreting and weighting estimates

The estimates used in the meta-analysis are not always readily available in the studies shown in Table 2. In Appendix B Table 9, we describe for each paper how we interpret the estimates and how they are converted to a common estimate (the relative effect of lockdowns on COVID-19 mortality) which is comparable across all studies.

Following Paldam (2015) and Stanley and Doucouliagos (2010), we also convert standard errors[32] and use the precision of each estimate (defined as 1/SE) to calculate the precision-weighted average of all estimates and present funnel plots. The precision-weighted average is our primary indicator of the efficacy of lockdowns, but we also report arithmetic averages and medians in the meta-analysis.

In the following sections, we present the meta-analysis for each of the three groups of studies (stringency index-studies, SIPO-studies, and studies analyzing specific NPIs).

4.1 Stringency index studies

Seven eligible studies examine the link between lockdown stringency and COVID-19 mortality. The results from these studies, converted to common estimates, are presented in Table 3 below. All studies are based on the COVID-19 Government Response Tracker's (OxCGRT) stringency index of Oxford University's Blavatnik School of Government (Hale et al. (2020)).

The OxCGRT stringency index neither measures the expected effectiveness of the lockdowns nor the expected costs. Instead, it describes the stringency based on nine equally weighted parameters.[33] Many countries followed similar patterns and almost all countries closed schools,

[32] Standard errors are converted such that the t-value, calculated based on common estimates and standard errors, is unchanged. When confidence intervals are reported rather than standard errors, we calculate standard errors using t-distribution with ∞ degrees of freedom (i.e. 1.96 for 95% confidence interval).

[33] The nine parameters are "C1 School closing," "C2 Workplace closing," "C3 Cancel public events," "C4 Restrictions on gatherings," "C5 Close public transport," "C6 Stay at home requirements," "C7 Restrictions on internal movement," "C8 International travel controls" and "H1 Public information campaigns." The latter, "H1

while only a few countries issued SIPOs without closing businesses. Hence, it is reasonable to perceive the stringency index as continuous, although not necessarily linear. The index includes recommendations (e.g. "workplace closing" is 1 if the government recommends closing (or work from home), cf. Hale et al. (2021)), but the effect of including recommendations in the index is primarily to shift the index parallelly upward and should not alter the results relative to our focus on mandated NPIs. It is important to note that the index is not perfect. As pointed out by Book (2020), it is certainly possibly to identify errors and omissions in the index. However, the index is objective and unbiased and as such, useful for cross-sectional analysis with several observations, even if not suitable for comparing the overall strictness of lockdowns in two countries.

Since the studies examined use different units of estimates, we have created common estimates for Europe and United States to make them comparable. The common estimates show the effect of the average lockdown in Europe and United States (with average stringencies of 76 and 74, respectively, between March 16th and April 15th, 2020, compared to a policy based solely on recommendations (stringency 44)). For example, Ashraf (2020) estimates that the effect of stricter lockdowns is -0.073 to -0.326 deaths/million per stringency point. We use the average of these two estimates (-0.200) in the meta-analysis (see Table 9 in Appendix B for a description for all studies). The average lockdown in Europe between March 16th and April 15th, 2020, was 32 points stricter than a policy solely based on recommendations (76 vs. 44). In United States, it was 30 points. Hence, the total effect of the lockdowns compared to the recommendation policy was -6.37 deaths/million in Europe (32 x -0.200) and -5.91 deaths/million in United States. With populations of 748 million and 333 million, respectively the total effect as estimated by Ashraf (2020) is 4,766 averted COVID-19 deaths in Europe and 1,969 averted COVID-19 deaths in United States. By the end of the study period in Ashraf (2020), which is May 20, 2020, 164,600 people in Europe and 97,081 people in the United States had died of COVID-19. Hence, the 4,766 averted COVID-19 deaths in Europe and the 1,969 averted COVID-19 deaths in the United States corresponds to 2.8% and 2.0% of all COVID-19 deaths, respectively, with an arithmetic average of 2.4%. Our common estimate is thus -2.4%, cf. Table 3. So, this means that Ashraf (2020) estimates that without lockdowns, COVID-19 deaths in Europe would have been 169,366 and COVID-19 deaths in the U.S. would have been 99,050. Our approach is not unproblematic. First of all, the level of stringency varies over time for all countries. We use the stringency between March 16th and April 15th, 2020 because this period covers the main part of the first wave which most of the studies analyze. Secondly, OxCGRT has changed the index over time and a 10-point difference today may not be exactly the same as a 10-point difference when the studies were finalized. However, we believe these problems are unlikely to significantly alter our results.

Public information campaigns," is not an intervention following our definition, as it is not a mandatory requirement. However, of 97 European countries and U.S. States in the OxCGRT database, only Andorra, Belarus, Bosnia and Herzegovina, Faeroe Islands, and Moldova – less than 1.6% of the population – did not get the maximum score by March 20, 2020, so the parameter simply shifts the index parallelly upward and should not have notable impact on the analyzes.

Table 3 demonstrates that the studies find that lockdowns, on average, have reduced COVID-19 mortality rates by 0.2% (precision-weighted). The results yield a median of -2.4% and an arithmetic average of -7.3%. Only one of the seven studies, Fuller et al. (2021), finds a significant *and* (relative to the effect predicted in studies like Ferguson et al. (2020)) substantial effect of lockdowns (-35%). The other six studies find much smaller effects. Hence, based on the stringency index studies, we find little to no evidence that mandated lockdowns in Europe and the United States had a noticeable effect on COVID-19 mortality rates. And, as will be discussed in the next paragraph, the fifth column of Table 3 displays the number of quality dimensions (out of 4) met by each study.

Table 3: Overview of common estimates from studies based on stringency indexes

Effect on COVID-19 mortality	Estimate (Estimated Averted Deaths / Total Deaths)	Standard error	Weight (1/SE)	Quality dimensions
Bjørnskov (2021)	-0.3%	0.8%	119	3
Shiva and Molana (2021)	-4.1%	0.4%	248	4
Stockenhuber (2020)*	0.0%	n/a	n/a	3
Chisadza et al. (2021)	0.1%	0.0%	7,390	4
Goldstein et al. (2021)	-9.0%	3.8%	26	2
Fuller et al. (2021)	-35.3%	9.1%	11	2
Ashraf (2020)	-2.4%	0.4%	256	2
Precision-weighted average (arithmetic average / median)	**-0.2% (-7.3%/-2.4%)**			

Note: The table shows the estimates for each study converted to a common estimate, i.e. the implied effect on COVID-19 mortality in Europe and United States. A negative number corresponds to fewer deaths, so -5% means 5% lover COVID-19 mortality. For studies which report estimates in deaths per million, the common estimate is calculated as: (COVID-19 mortality with "common area's" policy) / (COVID-19 mortality with recommendation policy) -1, where (COVID-19 mortality with recommendation policy) is calculated as ((COVID-19 mortality with "common area's" policy) - Estimate x Difference in stringency x population). Stringencies in Europe and United States are equal to the average stringency from March 16th to April 15th 2020 (76 and 74 respectively) and the stringency for the policy based solely on recommendations is 44 following Hale et al. (2020). For the conversion of other studies see Table 9 in appendix B.

** It is not possible to calculate a common estimate for Stockenhuber (2020). When calculating arithmetic average / median, the study is included as 0%, because estimates are insignificant and signs of estimates are mixed (higher strictness can cause both lower and higher COVID-19 mortality).*

We now turn to the quality dimensions. Table 4 presents the results differentiated by the four quality dimensions. Two studies, Shiva and Molana (2021) and Chisadza et al. (2021), meet all quality dimensions. The precision-weighted average for these studies is 0.0%, meaning that lockdowns had no effect on COVID-19 mortality. Two studies live up to 3 of 4 quality dimensions (Bjørnskov (2021a) and Stockenhuber (2020)). The precision-weighted average for these studies is -0.3%, meaning that lockdowns reduced COVID-19 mortality by 0.3%. Three studies lack at least two quality dimensions.[34] These studies find that lockdowns reduce COVID-19 mortality by 4.2%. To sum up, we find that the studies that meet at least 3 of 4 quality measures find that lockdowns have little to no effect on COVID-19 mortality, while studies that

[34] In fact, the working papers by P. Goldstein et al. (2021), Fuller et al. (2021) and Ashraf (2020) all lack exactly two quality parameters.

meet 2 of 4 quality measures find a small effect on COVID-19 mortality. These results are far from those estimated with the use of epidemiological models, such as the Imperial College London (Ferguson et al. (2020).

Table 4: Overview of common estimates split on quality dimensions for studies based on stringency indexes

Values show effect on COVID-19 mortality	Precision-weighted average*	Arithmetic average	Median
Peer-reviewed vs. working papers			
Peer-reviewed [4]	0.0%	-1.1%	-0.2%
Working paper [3]	-4.2%	-15.6%	-9.0%
Long vs. short time period			
Data series ends after 31 May 2020 [6]	-0.1%	-8.1%	-0.2%
Data series ends before 31 May 2020 [1]	-2.4%	-2.4%	-9.0%
No early effect on mortality			
Does not find an effect within the first 14 days (including n/a) [5]	-0.2%	-8.3%	-2.4%
Finds effect within the first 14 days [2]	-1.9%	-4.7%	-4.7%
Social sciences vs. other sciences			
Social sciences [5]	-0.1%	-3.1%	-2.4%
Other sciences [2]	-35.3%	-17.7%	-17.7%
4 of 4 quality dimensions [2]	**0.0%**	**-2.0%**	**-2.0%**
3 of 4 quality dimensions [2]	**-0.3%**	**-0.2%**	**-0.2%**
2 of 4 quality dimensions or fewer [3]	**-4.2%**	**-15.6%**	**-9.0%**

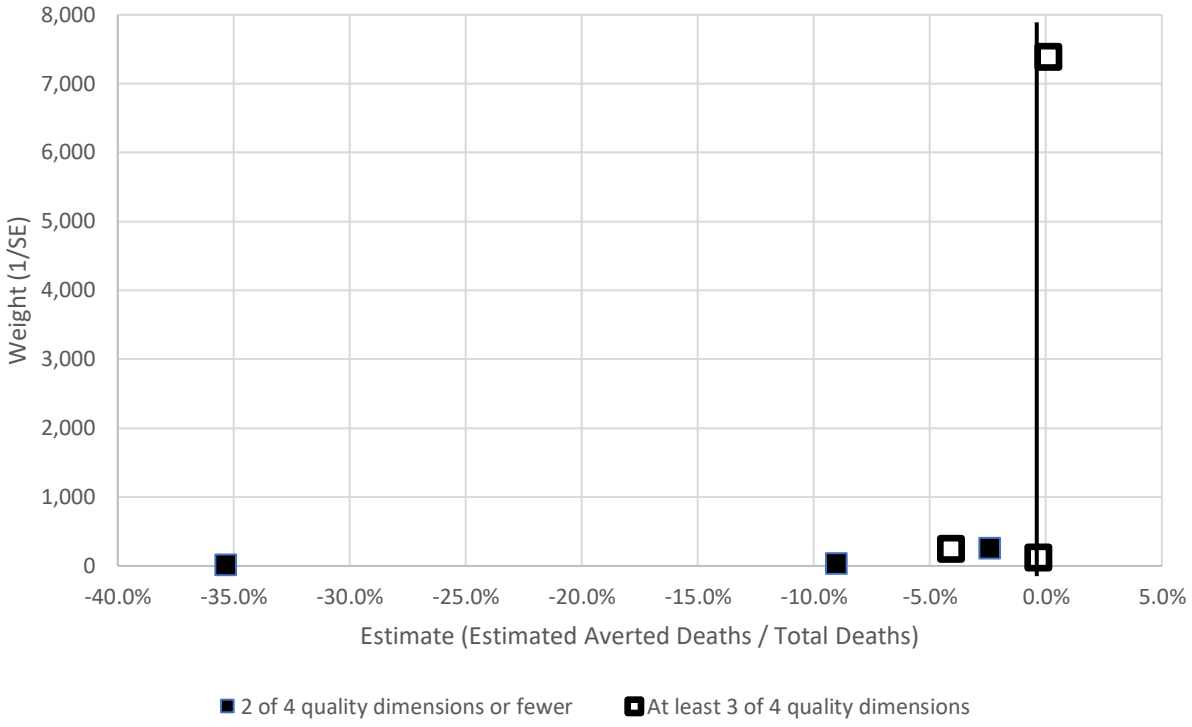
*Note: The table shows the common estimate as described in Table 3 for each quality dimension. The number of studies in each category is in square brackets. * The precision-weighted average does not include studies where no common standard error is available, cf. Table 3.*

Figure 5 shows a funnel plot for the studies in Table 3, except Stockenhuber (2020), where common estimate standard errors cannot be derived. Chisadza et al. (2021) has a far higher precision than the other studies (1/SE is 7,398 and the estimate is 0.1%)[35], and there are indications that the estimate from Fuller et al. (2021) (the bottom left) is an imprecise outlier.[36] Figure 5 The plot also shows that the studies with at least 3 of 4 quality dimensions are centered around zero and generally have higher precision than other studies.

[35] Excluding Chisadza et al. (2021) from the precision-weighted average changes the average to -3.5%.

[36] Excluding Fuller et al. (2021) from the precision-weighted average only marginally changes the average because the precision is very low.

Figure 5: Funnel plot for estimates from studies based on stringency indexes



Note: The figure displays all estimates and the precision of the estimate defined as one over the standard error. Studies where standard errors are not available are not included. Studies which live up to at least 3 of 4 quality dimensions are marked with white, while studies which lives up to 2 of 3 quality dimensions or less are marked with black. The vertical line illustrates the precision-weighted average.

Overall conclusion on stringency index studies

Compared to a policy based solely on recommendations, we find little evidence that lockdowns had a noticeable impact on COVID-19 mortality Only one study, Fuller et al. (2021), finds a substantial effect, while the rest of the studies find little to no effect. Indeed, according to stringency index studies, lockdowns in Europe and the United States reduced only COVID-19 mortality by 0.2% on average.

In the following section we will look at the effect of SIPOs. The section follows the same structure as this section.

4.2 Shelter-in-place order (SIPO) studies

We have identified 13 eligible studies which estimate the effect of Shelter-In-Place Orders (SIPOs) on COVID-19 mortality, cf. Table 5. Seven of these studies look at multiple NPIs of which a SIPO is just one, while six studies estimate the effect of a SIPO vs. no SIPO in the United States. According to the containment and closure policy indicators from OxCGRT, 41 states in the U.S. issued SIPOs in the spring of 2020. But usually, these were introduced after implementing other NPIs such as school closures or workplace closures. On average, SIPOs

were issued 7½ days after *both* schools and workplaces closed, and 12 days after the first of the two closed. Only one state, Tennessee, issued a SIPO before schools and workplaces closed. The 10 states that did not issue SIPOs all closed schools. Moreover, of those 10 states, three closed some non-essential businesses, while the remaining 7 closed all non-essential businesses. Because of this, we perceive estimates for SIPOs based on U.S.-data as the marginal effect of SIPOs on top of other restrictions, although we acknowledge that the estimates may capture the effects of other NPI measures as well.

The results of eligible studies based on SIPOs are presented in Table 5. The table demonstrates that the studies generally find that SIPOs have reduced COVID-19 mortality by 2.9% (on a precision-weighted average). There is an apparent difference between studies in which a SIPO is one of multiple NPIs, and studies in which a SIPO is the only examined intervention. The former group generally finds that SIPOs *increase* COVID-19 mortality *marginally*, whereas the latter finds that SIPOs *decrease* COVID-19 mortality. As we will see below, this difference could be explained by differences in the quality dimensions, and especially the time period covered by each study.

Table 5: Overview of estimates from studies based on SIPOs

Values show effect on COVID-19 mortality	Estimate (Estimated Averted Deaths / Total Deaths)	Standard error	Weight (1/SE)	Quality dimensions
Studies where SIPO is one of several examined interventions and not (as) likely to capture the effect of other interventions				
Chernozhukov et al. (2021)	-17.7%	14.3%	7	4
Chaudhry et al. (2020) *	0.0%	n/a	n/a	2
Aparicio and Grossbard (2021)	2.6%	2.8%	35	4
Stokes et al. (2020)	0.8%	11.1%	9	3
Spiegel and Tookes (2021)	13.1%	6.6%	15	3
Bonardi et al. (2020)	0.0%	n/a	n/a	1
Guo et al. (2021)	4.6%	14.8%	4	3
Average (median) where SIPO is one of several variables	2.8% (0.5%/0.8%)			
Studies where SIPO is the only examined intervention and may capture the effect of other interventions				
Sears et al. (2020)	-32.2%	17.6%	6	2
Alderman and Harjoto (2020)	-1.0%	0.6%	169	4
Berry et al. (2020)	1.1%	n/a	n/a	2
Fowler et al. (2021)	-35.0%	7.0%	14	2
Gibson (2020)	-6.0%	24.3%	4	4
Dave et al. (2020)	-40.8%	36.1%	3	3
Average (median) where SIPO is the only variable	-5.1% (-19.0%/-19.1%)			
Precision-weighted average (arithmetic average / median) for all studies	**-2.9% (-8.5%/0.0%)**			

*Note: * Chaudhry et al. (2020) does not provide an estimate but states that SIPO is insignificant. We use 0% when calculating the arithmetic average and median. Chaudhry et al. (2020) and Berry et al. (2021) do not affect the precision-weighted average, as we do not know the standard errors.*

Table 6 presents the results differentiated by quality dimensions. Four studies (Chernozhukov et al. (2021), Aparicio and Grossbard (2021), Alderman and Harjoto (2020) and Gibson (2020))

meet all quality dimensions but find vastly different effects of SIPOs on COVID-19 mortality. The precision weighted average of the four studies is -1.0%. Four studies meet 3 of 4 quality dimensions. They overall find that SIPOs *increase* COVID-19 mortality, as the precision-weighted average is positive (3.7%). The five studies that meet 2 of 4 quality dimensions or fewer[37] find a substantial reduction in COVID-19-mortality (-34.2%). This substantial reduction seems to be driven by relatively short data series. The latest data point for the three studies which find large effects of lockdowns (Sears et al. (2020), Fowler et al. (2021), and Dave et al. (2021)) are April 29, May 7, and April 20, respectively. This may indicate that SIPOs can delay deaths but not eliminate them completely. Disregarding these studies with short data series, the precision-weighted average is -0.1%.

Table 6: Quality dimensions for studies based on SIPOs

Values show effect on COVID-19 mortality	Precision-weighted average*	Arithmetic average	Median
Peer-reviewed vs. working papers			
Peer-review [10]	-2.4%	-7.9%	-0.5%
Working paper [3]	-12.0%	-10.5%	0.0%
Long vs. short time period			
Data serie ends after 31 May 2020 [6]	-0.1%	-1.4%	-0.1%
Data serie ends before 31 May 2020 [7]	-25.9%	-14.6%	0.0%
No early effect on mortality			
Finds effect within the first 14 days [9]	-2.0%	-10.0%	-1.0%
Does not find an effect within the first 14 days (including n/a) [4]	-10.3%	-5.2%	0.0%
Social sciences vs. other sciences			
Social sciences [12]	-2.9%	-9.2%	-0.5%
Other sciences [1]	n/a	0.0%	0.0%
4 of 4 quality dimensions [4]	-1.0%	-5.5%	-3.5%
3 of 4 quality dimensions [4]	3.7%	-5.6%	2.7%
2 of 4 quality dimensions or fewer [5]	-34.2%	-13.2%	0.0%

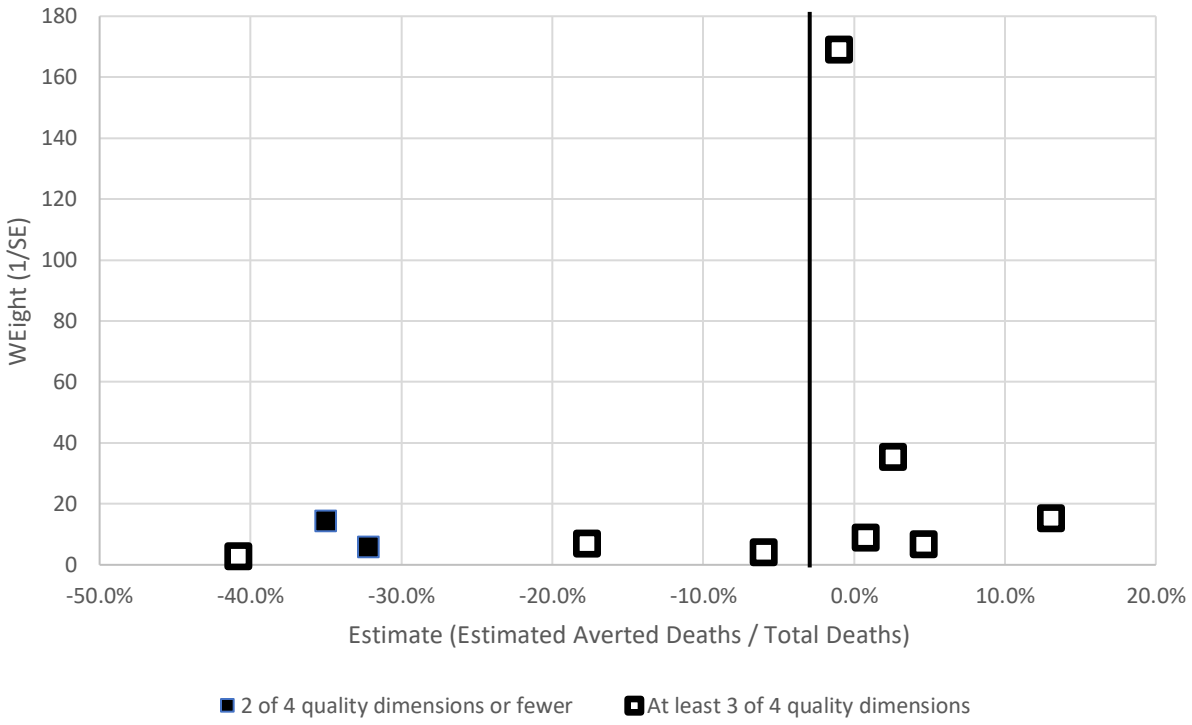
*Note: The table shows the common estimate as described in Table 5 for each quality dimension. The number of studies in each category is in square brackets. * The precision-weighted average does not include studies where no common standard error is available, cf. Table 5.*

Figure 6 shows a funnel plot for the studies in Table 5, except Chaudhry et al. (2020) and Berry et al. (2021), where common standard errors cannot be derived. Sears et al. (2020) stands out with a precision far higher than those of the other studies. But generally, the precisions of the studies are low and the estimates are placed on both sides of the zero-line with some 'tail' to the

[37] Bonardi et al. (2020) only meet one quality dimension (social science).

left.[38] Figure 5 also shows that four of eight studies with at least 3 of 4 quality dimensions find that SIPOs *increase* COVID-19 mortality by 0.8% to 13.1%.

Figure 6: Funnel plot for estimates from SIPO studies



Note: The figure displays all estimates and the precision of the estimate defined as one over the standard error. Studies where standard errors are not available are not included. Studies which live up to at least 3 of 4 quality dimensions are marked with white, while studies which lives up to 2 of 4 quality dimensions or less are marked with black. The vertical line illustrates the precision-weighted average.

Overall conclusion on SIPO studies

We find no clear evidence that SIPOs had a noticeable impact on COVID-19 mortality. Some studies find a large negative relationship between lockdowns and COVID-19 mortality, but this seems to be caused by short data series which does not cover a full COVID-19 'wave'. Several studies find a small positive relationship between lockdowns and COVID-19 mortality. Although this appears to be counterintuitive, it could be the result of an (asymptomatic) infected person being isolated at home under a SIPO can infect family members with a higher viral load causing more severe illness.[39] The overall effect measured by the precision-weighted average is -2.9%. The result is in line with Nuzzo et al. (2019), who state that "In the context of a high-impact

[38] This could indicate some publication bias, but the evidence is weak and with only 13 estimates, this cannot be formally tested

[39] E.g. see Guallar et al. (2020), who concludes, "Our data support that a greater viral inoculum at the time of SARS-CoV-2 exposure might determine a higher risk of severe COVID-19."

respiratory pathogen, quarantine may be the least likely NPI to be effective in controlling the spread due to high transmissibility" and World Health Organization Writing Group (2006), who conclude that "forced isolation and quarantine are ineffective and impractical."[40]

In the following section, we will look at the effect found in studies analyzing specific NPIs.

4.3 Studies of specific NPIs

A total of 11 eligible studies look at (multiple) specific NPIs independently or simply lockdown vs. no lockdown.[41] The definition of the specific NPIs varies from study to study and are somewhat difficult to compare. The variety in the definitions can be seen in the analysis of non-essential business closures and bar/restaurant closures. Chernozhukov et al. (2021) focus on a combined parameter (the average of business closure and bar/restaurant closure in each state), Aparicio and Grossbard (2021) look at business closure but not bar/restaurant closure, Spiegel and Tookes (2021) examine bar/restaurant closure but not business closure, and Guo et al. (2021) look at both business closures and bar/restaurant closures independently.

Some studies include several NPIs (e.g. Stokes et al. (2020) and Spiegel and Tookes (2021)), while others cover very few. Bongaerts et al. (2021) only study business closures, and Leffler et al. (2020) look at internal lockdown and international travel restrictions). Few NPIs in a model are potentially a problem because they can capture the effect of excluded NPIs. On the other hand, several NPIs in a model increase the risk of multiple test bias.

The differences in the choice of NPIs and in the number of NPIs make it challenging to create an overview of the results. In Table 7, we have merged the results in six overall categories but note that the estimates may not be fully comparable across studies. In particular, the lockdown-measure varies from study to study and in some cases is poorly defined by the authors. Also, there are only a few estimates within some of the categories. For instance, the estimate of the effect of facemasks is based on only two studies.

Table 7 illustrates that generally there is no evidence of a noticeable relationship between the most-used NPIs and COVID-19. Overall, lockdowns and limiting gatherings seem to increase COVID-19 mortality, although the effect is modest (0.6% and 1.6%, respectively) and border closures has little to no effect on COVID-19 mortality, with a precision-weighted average of -0.1% (removing the imprecise outlier from Guo et al. (2021) changes the precision-weighted average to -0.2%). We find a small effect of school closure (-4.4%), but this estimate is mainly driven by Auger et al. (2020), who – as noted earlier – use an "interrupted time series study"

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[40] Both Nuzzo et al. (2019) and World Health Organization Writing Group (2006) focus on quarantining infected persons. However, if quarantining infected persons is not effective, it should be no surprise that quarantining uninfected persons could be ineffective too.

[41] Note that we – according to our search strategy – did not search on specific measures such as "school closures" but on words describing the overall political approach to the COVID-19 pandemic such as "non-pharmaceutical," "NPIs," "lockdown" etc.

approach and may capture other effects such as seasonal and behavioral effects. The absence of a notable effect of school closures is in line with Irfan et al. (2021), who – based on a systematic review and meta-analysis of 90 published or preprint studies of transmission in children – concluded that "risks of infection among children in educational-settings was lower than in communities. Evidence from school-based studies demonstrate it is largely safe for young children (<10 years of age) to be at schools; however, older children (between 10 and 19 years of age) might facilitate transmission." UNICEF (2021) and ECDC (2020) reach similar conclusions.[42]

Mandating facemasks – an intervention that was not widely used in the spring of 2020, and in many countries was even discouraged – seems to have a large effect (-21.2%), but this conclusion is based on only two studies.[43] Again, our categorization may play a role, as the larger mask-estimate from Chernozhukov et al. (2021) is in fact "employee facemasks," not a general mask mandate. Our findings are somewhat in contrast to the result found in a review by Liu et al. (2021), who conclude that "fourteen of sixteen identified randomized controlled trials comparing face masks to no mask controls failed to find statistically significant benefit in the intent-to-treat populations." Similarly, a pre-COVID Cochrane review concludes, "There is low certainty evidence from nine trials (3507 participants) that wearing a mask may make little or no difference to the outcome of influenza-like illness (ILI) compared to not wearing a mask (risk ratio (RR) 0.99, 95% confidence interval (CI) 0.82 to 1.18). There is moderate certainty evidence that wearing a mask probably makes little or no difference to the outcome of laboratory-confirmed influenza compared to not wearing a mask (RR 0.91, 95% CI 0.66 to 1.26; 6 trials; 3005 participants)" (Jefferson et al. (2020)).[44] However, it should be noted that even if no effect is found in controlled settings, this does not necessarily imply that mandated face masks does not reduce mortality, as other factors may play a role (e.g. wearing a mask may function as a tax on socializing if people are bothered by wearing a face masks when they are socializing).

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[42] UNICEF (2021) concludes, "The preliminary findings thus far suggest that in-person schooling – especially when coupled with preventive and control measures – had lower secondary COVID-19 transmission rates compared to other settings and do not seem to have significantly contributed to the overall community transmission risks." Whereas, ECDC (2020) conclude, "School closures can contribute to a reduction in SARS-CoV-2 transmission, but by themselves are insufficient to prevent community transmission of COVID-19 in the absence of other nonpharmaceutical interventions (NPIs) such as restrictions on mass gathering," and states, "There is a general consensus that the decision to close schools to control the COVID-19 pandemic should be used as a last resort. The negative physical, mental health and educational impact of proactive school closures on children, as well as the economic impact on society more broadly, would likely outweigh the benefits."

[43] Note again, that we – according to our search strategy – did not search on the specific measures such as "masks," "face masks," "surgical masks" but on words describing the overall political approach to the COVID-19 pandemic such as "non-pharmaceutical," "NPIs," "lockdown" etc. Thus, we do not include most of the studies in mask reviews such as Liu et al. (2021) and Jefferson et al. (2020).

[44] Lipp and Edwards (2014) also find no evidence of an effect and – looking at disposable surgical face masks for preventing surgical wound infection in clean surgery – conclude, "Three trials were included, involving a total of 2113 participants. There was no statistically significant difference in infection rates between the masked and unmasked group in any of the trials." Meanwhile, Li et al. (2021) – based on six case-control studies – conclude, "In general, wearing a mask was associated with a significantly reduced risk of COVID-19 infection (OR = 0.38, 95% CI: 0.21-0.69, I^2 = 54.1%).

Only business closure consistently shows evidence of a negative relationship with COVID-19 mortality, but the variation in the estimated effect is large. Three studies find little to no effect, and three find large effects. Two of the larger effects are related to closing bars and restaurants. The "close business" category in Chernozhukov et al. (2021) is an average of closed businesses, restaurants, and movie theaters, while that same category is "closing restaurants and bars" in Spiegel and Tookes (2021). The last study finding a large effect is Bongaerts et al. (2021), the only eligible single-country study.[45]

As a final observation on Table 7, studies with fewer quality dimensions seem to find larger effects, but the pattern is not systematic.[46]

Table 7: Overview of estimates from studies of specific NPIs

	Lockdown (complete/ partial)	Facemasks/ Employee face masks	Business closure (/bars & restaurants)	Border closure (/quarantine)	School closures	Limiting gatherings	Quality dimensions
Chernozhukov et al. (2021)		-34.0%	-28.6%				4
Bongaerts et al. (2021)			-31.6%				2
Chaudhry et al. (2020)*	0.0%			0.0%			2
Toya & Skidmore (2021)	0.5%			-0.1%			3
Aparicio & Grossbard (2021)			-1.3%		0.5%	0.8%	4
Auger et al. (2020)					-58.0%		2
Leffler et al. (2020)	1.7%			-15.6%			2
Stokes et al. (2020)			0.3%	-24.6%	-0.1%	-6.3%	3
Spiegel & Tookes (2021)		-13.5%	-50.2%			11.8%	3
Bonardi et al. (2020)*	0.0%			0.0%			1
Guo et al. (2021)			-0.4%	36.3%	-0.2%	5.7%	3
Precision-weighted average	**0.6%**	**-21.2%**	**-10.6%**	**-0.1%**	**-4.4%**	**1.6%**	
Arithmetic average	**0.6%**	**-23.8%**	**-18.6%**	**-0.7%**	**-14.4%**	**3.0%**	
Median	**0.3%**	**-23.8%**	**-14.9%**	**0.0%**	**-0.1%**	**3.2%**	
4 of 4 quality dimensions	**n/a [0]**	**-34.0% [1]**	**-2.9% [2]**	**n/a [0]**	**0.5% [1]**	**0.8% [1]**	
3 of 4 quality dimensions	**0.5% [1]**	**-13.5% [1]**	**-21.5% [3]**	**0.0% [3]**	**-0.1% [2]**	**5.6% [3]**	
2 of 4 quality dimensions or fewer	**1.7% [2]**	**n/a [1]**	**-31.6% [2]**	**-15.6% [2]**	**-58.0% [1]**	**n/a [1]**	

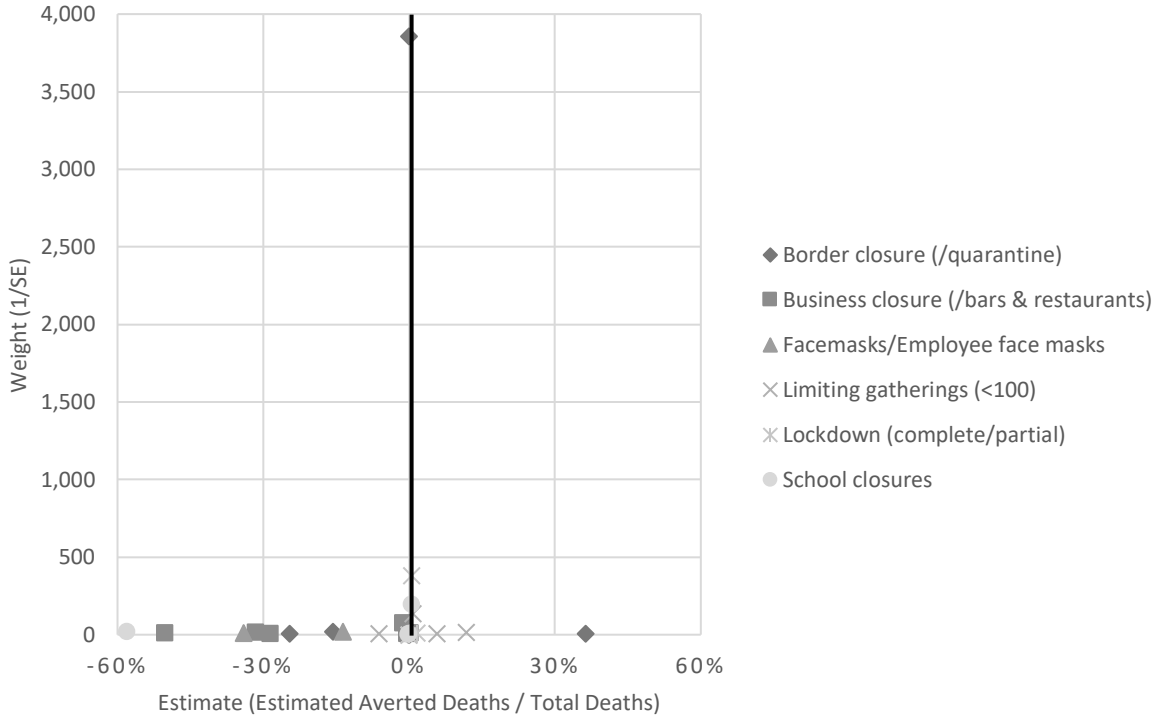
*Note: * It is not possible to derive common estimates and standard errors from Chaudhry et al. (2020) and Bonardi et al. (2020). Chaudhry et al. (2020) states that the effect of the various NPIs is insignificant without listing the estimates and standard errors. Bonardi et al. (2020) states that partial or regional lockdowns are as effective as stricter NPIs but does not provide information to calculate common estimates. Instead, we assume the estimate is 0% when calculating arithmetic average and median, while the estimates are excluded from the calculation of precision-weighted averages because there are no standard errors.*

[45] Bongaerts et al. (2021) (implicitly) assume that municipalities with different exposures to closed sectors are not inherently different, which may be a relatively strong assumption and could potentially drive their results.

[46] We saw with SIPOs that studies based on short data series tended to find larger effects than studies based on short data series. This is also somewhat true for studies examining multiple specific measures. If we focus on studies with long data series (>May 31st, 2020), the precision-weighted estimates are as follows (average for all studies in parentheses for easy comparison): Lockdown (complete/partial): 0.5% (0.6%), Facemasks/Employee face masks: -21.2% (-21.2%), Business closures (/bars & restaurants): -8.1% (-10.6%), Border closures (/quarantine): -0.1% (-0.1%), School closures: 0.5% (-4.4%), Limiting gatherings: 1.4% (1.6%).

Figure 7 shows a funnel plot for all estimates in Table 7, except Chaudhry et al. (2020) and Bonardi et al. (2020), where common standard errors cannot be derived. Two estimates from Toya and Skidmore (2020) stands out with a precision far higher than those of other studies, and estimates are placed with some 'tail' to the left, which could indicate some publication bias, i.e. reluctance to publish results that show large positive (more deaths) effects of lockdowns. The most precise estimates are gathered around 0%, while less precise studies are spread out between -58% and 36%. The precision-weighted average of all estimates across all NPIs is -0.6%.

Figure 7: Funnel plot for estimates from studies of specific NPIs



Note: The figure displays all estimates except two (se text in figure) of specific NPIs and the precision of the estimate defined as one over the standard error. Studies where standard errors are not available are not included.

Overall conclusion on specific NPIs

Because of the heterogeneity in NPIs across studies, it is difficult to draw strong conclusions based on the studies of multiple specific measures. We find no evidence that lockdowns, school closures, border closures, and limiting gatherings have had a noticeable effect on COVID-19 mortality. There is some evidence that business closures reduce COVID-19 mortality, but the variation in estimates is large and the effect seems related to closing bars. There may be an effect of mask mandates, but just two studies look at this, one of which one only looks at the effect of employee mask mandates.

5 Concluding observations

Public health experts and politicians have – based on forecasts in epidemiological studies such as that of Imperial College London (Ferguson et al. (2020) – embraced compulsory lockdowns as an effective method for arresting the pandemic. But, have these lockdown policies been effective in curbing COVID-19 mortality? This is the main question answered by our meta-analysis.

Adopting a systematic search and title-based screening, we identified 1,048 studies published by July 1st, 2020, which potentially look at the effect of lockdowns on mortality rates. To answer our question, we focused on studies that examine the actual impact of lockdowns on COVID-19 mortality rates based on registered cross-sectional mortality data and a counterfactual difference-in-difference approach. Out of the 1,048 studies, 34 met our eligibility criteria.

Conclusions

Overall, our meta-analysis fails to confirm that lockdowns have had a large, significant effect on mortality rates. Studies examining the relationship between lockdown strictness (based on the OxCGRT stringency index) find that the average lockdown in Europe and the United States only reduced COVID-19 mortality by 0.2% compared to a COVID-19 policy based solely on recommendations. Shelter-in-place orders (SIPOs) were also ineffective. They only reduced COVID-19 mortality by 2.9%.

Studies looking at specific NPIs (lockdown vs. no lockdown, facemasks, closing non-essential businesses, border closures, school closures, and limiting gatherings) also find no broad-based evidence of noticeable effects on COVID-19 mortality. However, closing non-essential businesses seems to have had some effect (reducing COVID-19 mortality by 10.6%), which is likely to be related to the closure of bars. Also, masks may reduce COVID-19 mortality, but there is only one study that examines universal mask mandates. The effect of border closures, school closures and limiting gatherings on COVID-19 mortality yields precision-weighted estimates of -0.1%, -4.4%, and 1.6%, respectively. Lockdowns (compared to no lockdowns) also do not reduce COVID-19 mortality.

Discussion

Overall, we conclude that lockdowns are not an effective way of reducing mortality rates during a pandemic, at least not during the first wave of the COVID-19 pandemic. Our results are in line with the World Health Organization Writing Group (2006), who state, “Reports from the 1918 influenza pandemic indicate that social-distancing measures did not stop or appear to dramatically reduce transmission […] In Edmonton, Canada, isolation and quarantine were instituted; public meetings were banned; schools, churches, colleges, theaters, and other public gathering places were closed; and business hours were restricted without obvious impact on the epidemic.” Our findings are also in line with Allen's (2021) conclusion: “The most recent research has shown that lockdowns have had, at best, a marginal effect on the number of Covid-19 deaths.” Poeschl and Larsen (2021) conclude that “interventions are generally effective in

mitigating COVID-19 spread". But, 9 of the 43 (21%) results they review find "no or uncertain association" between lockdowns and the spread of COVID-19, suggesting that evidence from that own study contradicts their conclusion.

The findings contained in Johanna et al. (2020) are in contrast to our own. They conclude that "for lockdown, ten studies consistently showed that it successfully reduced the incidence, onward transmission, and mortality rate of COVID-19." The driver of the difference is three-fold. First, Johanna et al. include modelling studies (10 out of a total of 14 studies), which we have explicitly excluded. Second, they included interrupted time series studies (3 of 14 studies), which we also exclude. Third, the only study using a difference-in-difference approach (as we have done) is based on data collected before May 1st, 2020. We should mention that our results indicate that early studies find relatively larger effects compared to later studies.

Our main conclusion invites a discussion of some issues. Our review does not point out *why* lockdowns did not have the effect promised by the epidemiological models of Imperial College London (Ferguson et al. (2020). We propose four factors that might explain the difference between our conclusion and the view embraced by some epidemiologists.

First, people respond to dangers outside their door. When a pandemic rages, people believe in social distancing regardless of what the government mandates. So, we believe that Allen (2021) is right, when he concludes, "The ineffectiveness [of lockdowns] stemmed from individual changes in behavior: either non-compliance or behavior that mimicked lockdowns." In economic terms, you can say that the demand for costly disease prevention efforts like social distancing and increased focus on hygiene is high when infection rates are high. Contrary, when infection rates are low, the demand is low and it may even be morally and economically rational not to comply with mandates like SIPOs, which are difficult to enforce. Herby (2021) reviews studies which distinguish between mandatory and voluntary behavioral changes. He finds that – on average – voluntary behavioral changes are 10 times as important as mandatory behavioral changes in combating COVID-19. If people voluntarily adjust their behavior to the risk of the pandemic, closing down non-essential businesses may simply reallocate consumer visits away from "nonessential" to "essential" businesses, as shown by Goolsbee and Syverson (2021), with limited impact on the total number of contacts.[47] This may also explain why epidemiological model simulations such as Ferguson et al. (2020) – which do not model behavior endogenously – fail to forecast the effect of lockdowns.

Second, mandates only regulate a fraction of our potential contagious contacts and can hardly regulate nor enforce handwashing, coughing etiquette, distancing in supermarkets, etc. Countries like Denmark, Finland, and Norway that realized success in keeping COVID-19 mortality rates relatively low allowed people to go to work, use public transport, and meet privately at home during the first lockdown. In these countries, there were ample opportunities to legally meet with others.

[47] In economic terms, lockdowns are substitutes for – not complements to – voluntary behavioral changes.

Third, even if lockdowns are successful in initially reducing the spread of COVID-19, the behavioral response may counteract the effect completely, as people respond to the lower risk by changing behavior. As Atkeson (2021) points out, the economic intuition is straightforward. If closing bars and restaurants causes the prevalence of the disease to fall toward zero, the demand for costly disease prevention efforts like social distancing and increased focus on hygiene also falls towards zero, and the disease will return.[48]

Fourth, unintended consequences may play a larger role than recognized. We already pointed to the possible unintended consequence of SIPOs, which may isolate an infected person at home with his/her family where he/she risks infecting family members with a higher viral load, causing more severe illness. But often, lockdowns have limited peoples' access to safe (outdoor) places such as beaches, parks, and zoos, or included outdoor mask mandates or strict outdoor gathering restrictions, pushing people to meet at less safe (indoor) places. Indeed, we do find some evidence that limiting gatherings was counterproductive and increased COVID-19 mortality.

One objection to our conclusions may be that we do not look at the role of timing. If timing is very important, differences in timing may empirically overrule any differences in lockdowns. We note that this objection is not necessarily in contrast to our results. If timing is very important relative to strictness, this suggests that well-timed, but very mild, lockdowns should work as well as, or better than, less well-timed but strict lockdowns. This is not in contrast to our conclusion, as the studies we reviewed analyze the effect of lockdowns compared but to doing very little (see Section 3.1 for further discussion). However, there is little solid evidence supporting the timing thesis, because it is inherently difficult to analyze (see Section 2.2 for further discussion). Also, even if it can be empirically stated that a well-timed lockdown is effective in combating a pandemic, it is doubtful that this information will ever be useful from a policy perspective.

But, what explains the differences between countries, if not differences in lockdown policies? Differences in population age and health, quality of the health sector, and the like are obvious factors. But several studies point at less obvious factors, such as culture, communication, and coincidences. For example, Frey et al. (2020) show that for the same policy stringency, countries with more obedient and collectivist cultural traits experienced larger declines in geographic mobility relative to their more individualistic counterpart. Data from Germany Laliotis and Minos (2020) shows that the spread of COVID-19 and the resulting deaths in predominantly Catholic regions with stronger social and family ties were much higher compared to non-Catholic ones at the local NUTS 3 level.[49]

Government communication may also have played a large role. Compared to its Scandinavian neighbors, the communication from Swedish health authorities was far more subdued and embraced the idea of public health vs. economic trade-offs. This may explain why Helsingen et

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[48] This kind of behavior response may also explain why Subramanian and Kumar (2021) find that increases in COVID-19 cases are unrelated to levels of vaccination across 68 countries and 2947 counties in the United States. When people are vaccinated and protected against severe disease, they have less reason to be careful.

[49] The NUTS classification (Nomenclature of territorial units for statistics) is a hierarchical system for dividing up the economic territory of the EU and the UK. There are 1215 regions at the NUTS 3-level.

al. (2020), found, based on questionnaire data collected from mid-March to mid-April, 2020, that even though the daily COVID-19 mortality rate was more than four times higher in Sweden than in Norway, Swedes were less likely than Norwegians to not meet with friends (55% vs. 87%), avoid public transportation (72% vs. 82%), and stay home during spare time (71% vs. 87%). That is, despite a more severe pandemic, Swedes were less affected in their daily activities (legal in both countries) than Norwegians.

Many other factors may be relevant, and we should not underestimate the importance of coincidences. An interesting example illustrating this point is found in Arnarson (2021) and Björk et al. (2021), who show that areas where the winter holiday was relatively late (in week 9 or 10 rather than week 6, 7 or 8) were hit especially hard by COVID-19 during the first wave because the virus outbreak in the Alps could spread to those areas with ski tourists. Arnarson (2021) shows that the effect persists in later waves. Had the winter holiday in Sweden been in week 7 or week 8 as in Denmark, the Swedish COVID-19 situation could have turned out very differently.[50]

Policy implications

In the early stages of a pandemic, before the arrival of vaccines and new treatments, a society can respond in two ways: mandated behavioral changes or voluntary behavioral changes. Our study fails to demonstrate significant positive effects of mandated behavioral changes (lockdowns). This should draw our focus to the role of voluntary behavioral changes. Here, more research is needed to determine how voluntary behavioral changes can be supported. But it should be clear that one important role for government authorities is to provide information so that citizens can voluntarily respond to the pandemic in a way that mitigates their exposure.

Finally, allow us to broaden our perspective after presenting our meta-analysis that focuses on the following question: "What does the evidence tell us about the effects of lockdowns on mortality?" We provide a firm answer to this question: The evidence fails to confirm that lockdowns have a significant effect in reducing COVID-19 mortality. The effect is little to none.

The use of lockdowns is a unique feature of the COVID-19 pandemic. Lockdowns have not been used to such a large extent during any of the pandemics of the past century. However, lockdowns during the initial phase of the COVID-19 pandemic have had devastating effects. They have contributed to reducing economic activity, raising unemployment, reducing schooling, causing political unrest, contributing to domestic violence, and undermining liberal democracy. These costs to society must be compared to the benefits of lockdowns, which our meta-analysis has shown are marginal at best. Such a standard benefit-cost calculation leads to a strong conclusion: lockdowns should be rejected out of hand as a pandemic policy instrument.

[50] Another case of coincidence is illustrated by Shenoy et al. (2022), who find that areas that experienced rainfall early in the pandemic realized fewer deaths because the rainfall induced social distancing.

6 Appendix A. The role of timing

Some of the included papers study the importance of the timing of lockdowns, while several other papers only looking at timing of (but not on the inherent effect of) lockdowns have been excluded from the literature list in this review. There's no doubt that being prepared for a pandemic and knowing when it arrives at your doorstep is vital. However, two problems arise with respect to imposing early lockdowns.

First of all, it was virtually impossible to determine the right timing when COVID-19 hit Europe and the United States. The World Health Organization declared the outbreak of a pandemic on 11 March 2020, but at that date Italy had already registered 13.7 COVID-19-deaths per million (all infected before approximately 22 February, because of the roughly 18 day gap between infection and death, c.f. e.g.. Bjørnskov (2021a)). On 29 March 2020, 18 days after WHO declared the outbreak a pandemic and the earliest a lockdown response to WHO's announcement could have an effect, the death toll in Italy was a staggering 178 COVID-19-deaths per million with an additionally 13 per million dying each day.

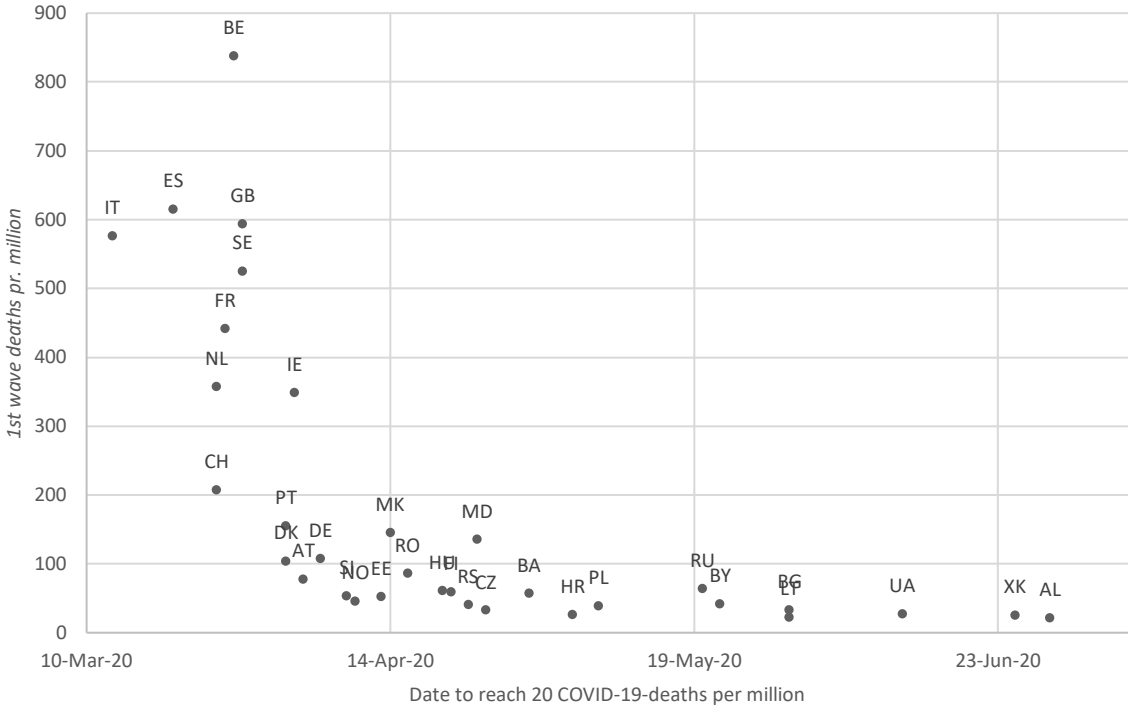
There are reasons to believe that many countries and regions were hit particularly hard during the first wave of COVID, because they had no clue about how bad it really was. This point is illustrated in Figure 8 (and Figure 9), which show that countries (and states), which were hit hard and early, experienced large death tolls compared to countries where the pandemic had a slower start. Björk et al. (2021) and Arnarson (2021) show that areas with a winter holiday in week 10 and – especially – week 9 were hit hard, because they imported cases from the Alps *before* they knew the pandemic was wide spread at the ski resorts. Hence, while acting early by warning citizens and closing business may be an effective strategy; this was not a feasible strategy for most countries in the spring of 2020.

The second problem is that it is extremely difficult to differentiate between the effect of public awareness and the effect of lockdowns. If people and politicians react to the same information, for example deaths in geographical neighboring countries (many EU-countries reacted to deaths in Italy) or in another part of the same country, the effect of lockdowns cannot easily be separated from the effect of voluntary social distancing or, use of hand sanitizers. Hence, we find it problematic to use national lockdowns and differences in the progress of the pandemic in different regions to say anything about the effect of early lockdowns on the pandemic, as the estimated effect might just as well come from voluntary behavior changes, when people in Southern Italy react to the situation in Northern Italy.

We have seen no studies which we believe credibly separate the effect of early lockdown from the effect of early voluntary behavior changes. Instead, the estimates in these studies capture the effects of lockdowns *and* voluntary behavior changes. As Herby (2021) illustrates, voluntary behavior changes are essential to a society's response to an pandemic and can account for up to 90% of societies' total response to the pandemic.

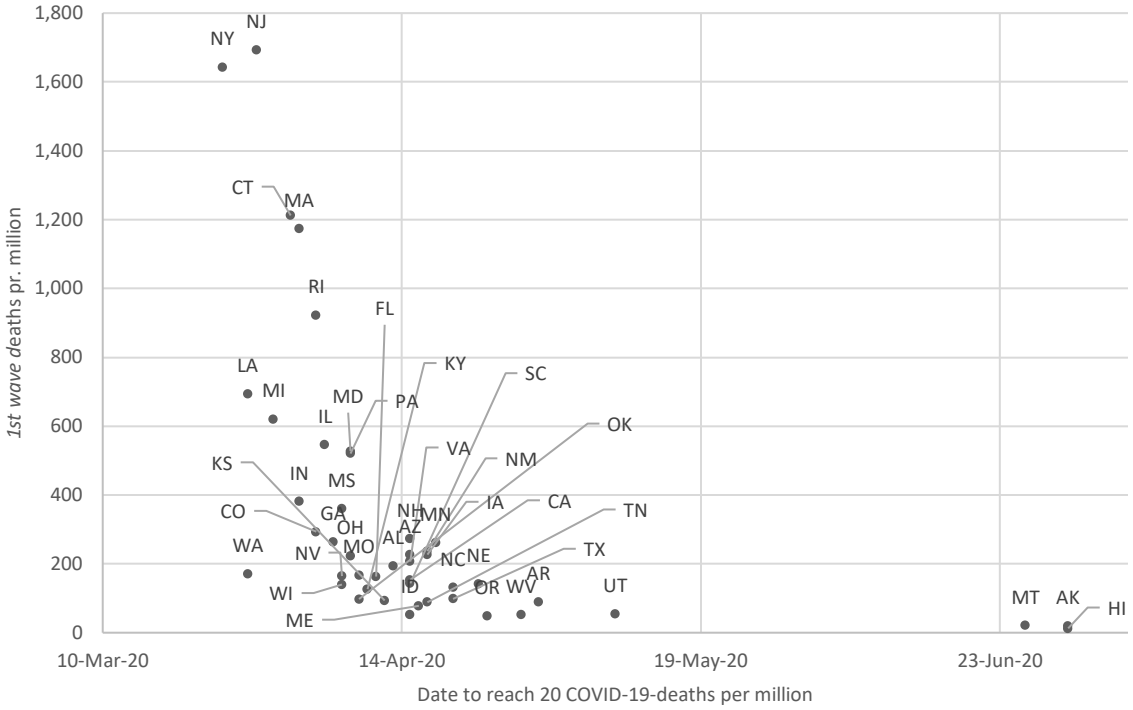
Including these studies will greatly overestimate the effect of lockdowns, and, hence, we chose not to include studies focusing on timing of lockdowns in our review.

Figure 8: Taken by surprise. The importance of having time to prepare in Europe



Description: European countries with more than one million citizens.
Source: Our World in Data

Figure 9: Taken by surprise. The importance of having time to prepare in U.S. states



Description: U.S. states with more than one million citizens.
Source: Our World in Data

7 Appendix B. Supplementary information

7.1 Excluded studies

Below is a list will the studies excluded during the eligibility phase of our identification process and a short description of our basis for excluding the study.

Table 8: Studies excluded during the eligibility phase of our identification process

1. Study (Author & title)	2. Reason for exclusion
Alemán et al. (2020); "Evaluating the effectiveness of policies against a pandemic"	Too few observations
Alshammari et al. (2021); "Are countries' precautionary actions against COVID-19 effective? An assessment study of 175 countries worldwide"	Is purely descriptive
Amuedo-Dorantes et al. (2020); "Timing is Everything when Fighting a Pandemic: COVID-19 Mortality in Spain"	Duplicate
Amuedo-Dorantes et al. (2021); "Early adoption of non-pharmaceutical interventions and COVID-19 mortality"	Only looks at timing
Amuedo-Dorantes, Kaushal and Muchow (2020); "Is the Cure Worse than the Disease? County-Level Evidence from the COVID-19 Pandemic in the United States"	Duplicate
Amuedo-Dorantes, Kaushal and Muchow (2021); "Timing of social distancing policies and COVID-19 mortality: county-level evidence from the U.S."	Only looks at timing
Arruda et al. (2021); "ASSESSING THE IMPACT OF SOCIAL DISTANCING ON COVID-19 CASES AND DEATHS IN BRAZIL: AN INSTRUMENTED DIFFERENCE-IN-	Social distancing (not
Bakolis et al. (2021); "Changes in daily mental health service use and mortality at the commencement and lifting of COVID-19 'lockdown' policy in 10 UK sites: a regression	Uses a time series approach
Bardey, Fernández and Gravel (2021); "Coronavirus and social distancing: do non-pharmaceutical-interventions work (at least) in the short run?"	Only looks at timing
Berardi et. Al. (2020); "The COVID-19 pandemic in Italy: policy and technology impact on health and non-health outcomes"	Too few observations
Bhalla (2020); "Lockdowns and Closures vs COVID–19: COVID Wins"	Uses modelling
Björk et al. (2021); "Impact of winter holiday and government responses on mortality in Europe during the first wave of the COVID-19 pandemic"	Only looks at timing
Bongaerts, Mazzola and Wagner (2020); "Closed for business"	Duplicate
Born, Dietrich and Müller (2021); "The lockdown effect: A counterfactual for Sweden"	Synthetic control study
Born, Dietrich and Müller (2021); "The lockdown effect: A counterfactual for Sweden"	Duplicate
Bushman et al. (2020); "Effectiveness and compliance to social distancing during COVID-19"	Social distancing (not
Castaneda and Saygili (2020); "The effect of shelter-in-place orders on social distancing and the spread of the COVID-19 pandemic: a study of Texas"	Uses a time series approach
Cerqueti et al. (2021); "The sooner the better: lives saved by the lockdown during the COVID-19 outbreak. The case of Italy"	Synthetic control study
Chernozhukov, Kasahara and Schrimpf (2021); "Mask mandates and other lockdown policies reduced the spread of COVID-19 in the U.S."	Duplicate
Chin et al. (2020); "Effects of non-pharmaceutical interventions on COVID-19: A Tale of Three Models"	Uses modelling
Cho (2020); "Quantifying the impact of nonpharmaceutical interventions during the COVID-19 outbreak: The case of Sweden"	Synthetic control study
Coccia (2020); "The effect of lockdown on public health and economic system: findings from first wave of the COVID-19 pandemic for designing effective strategies to cope	Only looks at timing
Coccia (2021); "Different effects of lockdown on public health and economy of countries: Results from first wave of the COVID-19 pandemic"	Too few observations
Conyon and Thomsen (2021); "COVID-19 in Scandinavia"	Synthetic control study
Conyon et al. (2020); "Lockdowns and COVID-19 deaths in Scandinavia"	Too few observations
Dave et al. (2020); "Did the Wisconsin Supreme Court restart a COVID-19 epidemic? Evidence from a natural experiment"	Synthetic control study
Delis, Iosifidi and Tasiou (2021); "Efficiency of government policy during the COVID-19 pandemic"	Do not look at mortality
Dreher et al. (2021); "Policy interventions, social distancing, and SARS-CoV-2 transmission in the United States: a retrospective state-level analysis"	Do not look at mortality
Duchemin, Veber and Boussau (2020); "Bayesian investigation of SARS-CoV-2-related mortality in France"	Uses modelling
Fair et. Al. (2021); "Estimating COVID-19 cases and deaths prevented by non-pharmaceutical interventions in 2020-2021, and the impact of individual actions: a retrospective	Uses modelling
Filias (2020); "The impact of government policies effectiveness on the officially reported deaths attributed to covid-19."	Student paper
Fowler et al. (2021); "Stay-at-home orders associate with subsequent decreases in COVID-19 cases and fatalities in the United States"	Duplicate
Friedson et al. (2020); "Did California's shelter-in-place order work? Early coronavirus-related public health effects"	Duplicate
Friedson et al. (2020); "Shelter-in-place orders and public health: evidence from California during the COVID-19 pandemic"	Synthetic control study
Fuss, Weizman and Tan (2020); "COVID19 pandemic: how effective are interventive control measures and is a complete lockdown justified? A comparison of countries and	Do not look at mortality
Ghosh, Ghosh and Narymanchi (2020); "A Study on The Effectiveness of Lock-down Measures to Control The Spread of COVID-19"	Synthetic control study
Glogowsky et al. (2021); "How Effective Are Social Distancing Policies? Evidence on the Fight Against COVID-19"	Only looks at timing
Glogowsky, Hansen and Schächtele (2020); "How effective are social distancing policies? Evidence on the fight against COVID-19 from Germany"	Duplicate
Glogowsky, Hansen and Schächtele (2020); "How Effective Are Social Distancing Policies? Evidence on the Fight Against COVID-19 from Germany"	Duplicate
Gordon, Grafton and Steinshamn (2021); "Cross-country effects and policy responses to COVID-19 in 2020: The Nordic countries"	Do not look at mortality
Gordon, Grafton and Steinshamn (2021); "Statistical Analyses of the Public Health and Economic Performance of Nordic Countries in Response to the COVID-19 Pandemic"	Too few observations
Guo et al. (2020); "Social distancing interventions in the United States: An exploratory investigation of determinants and impacts"	Duplicate
Huber and Langen (2020); "The impact of response measures on COVID-19-related hospitalization and death rates in Germany and Switzerland"	Duplicate
Huber and Langen (2020); "Timing matters: the impact of response measures on COVID-19-related hospitalization and death rates in Germany and Switzerland"	Only looks at timing
Jain et al. (2020); "A comparative analysis of COVID-19 mortality rate across the globe: An extensive analysis of the associated factors"	Do not look at mortality
Juranek and Zoutman (2021); "The effect of non-pharmaceutical interventions on the demand for health care and mortality: evidence on COVID-19 in Scandinavia"	Too few observations
Kakpo and Nuhu (2020); "Effects of Social Distancing on COVID-19 Infections and Mortality in the U.S."	Social distancing (not
Kapoor and Ravi (2020); "Impact of national lockdown on COVID-19 deaths in select European countries and the U.S. using a Changes-in-Changes model"	Too few observations
Khatiwada and Chalise (2020); "Evaluating the efficiency of the Swedish government policies to control the spread of Covid-19."	Student paper
Korevaar et al. (2020); "Quantifying the impact of U.S. state non-pharmaceutical interventions on COVID-19 transmission"	Do not look at mortality
Kumar et. Al. (2020); "Prevention-Versus Promotion-Focus Regulatory Efforts on the Disease Incidence and Mortality of COVID-19: A Multinational Diffusion Study Using	Do not look at mortality
Le et al. (2020); "Impact of government-imposed social distancing measures on COVID-19 morbidity and mortality around the world"	Uses a time series approach
Liang et al. (2020); "Covid-19 mortality is negatively associated with test number and government effectiveness"	Not effect of lockdowns
Mader and Rütternauer (2021); "The effects of non-pharmaceutical interventions on COVID-19-related mortality: A generalized synthetic control approach across 169 countries"	Synthetic control study
Matzinger and Skinner (2020); "Strong impact of closing schools, closing bars and wearing masks during the Covid-19 pandemic: results from a simple and revealing analysis"	Uses modelling
Mccafferty and Ashley (2020); "Covid-19 Social Distancing Interventions by State Mandate and their Correlation to Mortality in the United States"	Duplicate
Medline et al. (2020); "Evaluating the impact of stay-at-home orders on the time to reach the peak burden of Covid-19 cases and deaths: does timing matter?"	Only looks at timing

1. Study (Author & title)	2. Reason for exclusion
Mu et al. (2020); "Effect of social distancing interventions on the spread of COVID-19 in the state of Vermont"	Uses modelling
Nakamura (2020); "The Impact of Rapid State Policy Response on Cumulative Deaths Caused by COVID-19"	Student paper
Neidhöfer and Neidhöfer (2020); "The effectiveness of school closures and other pre-lockdown COVID-19 mitigation strategies in Argentina, Italy, and South Korea"	Synthetic control study
Oliveira (2020); "Does' Staying at Home'Save Lives? An Estimation of the Impacts of Social Isolation in the Registered Cases and Deaths by COVID-19 in Brazil"	Social distancing (not
Palladina et al. (2020); "Effect of Implementation of the Lockdown on the Number of COVID-19 Deaths in Four European Countries"	Uses a time series approach
Palladina et al. (2020); "Effect of timing of implementation of the lockdown on the number of deaths for COVID-19 in four European countries"	Duplicate
Palladino et al. (2020); "Excess deaths and hospital admissions for COVID-19 due to a late implementation of the lockdown in Italy"	Uses a time series approach
Peixoto et al. (2020); "Rapid assessment of the impact of lockdown on the COVID-19 epidemic in Portugal"	Uses modelling
Piovani et. Al. (2021); "Effect of early application of social distancing interventions on COVID-19 mortality over the first pandemic wave: An analysis of longitudinal data from 37	Only looks at timing
Reinbold (2021); "Effect of fall 2020 K-12 instruction types on CoViD-19 cases, hospital admissions, and deaths in Illinois counties"	Synthetic control study
Renne, Roussellet and Schwenkler (2020); "Preventing COVID-19 Fatalities: State versus Federal Policies"	Uses modelling
Siedner et al. (2020); "Social distancing to slow the U.S. COVID-19 epidemic: Longitudinal pretest–posttest comparison group study"	Duplicate
Siedner et al. (2020); "Social distancing to slow the U.S. COVID-19 epidemic: Longitudinal pretest–posttest comparison group study"	Uses a time series approach
Silva, Filho and Fernandes (2020); "The effect of lockdown on the COVID-19 epidemic in Brazil: evidence from an interrupted time series design"	Uses a time series approach
Stamam et al. (2020); "IMPACT OF LOCKDOWN MEASURE ON COVID-19 INCIDENCE AND MORTALITY IN THE TOP 31 COUNTRIES OF THE WORLD."	Uses a time series approach
Steinegger et al. (2021); "Retrospective study of the first wave of COVID-19 in Spain: analysis of counterfactual scenarios"	Only looks at timing
Stephens et al. (2020); "Does the timing of government COVID-19 policy interventions matter? Policy analysis of an original database."	Only looks at timing
Supino et al. (2020); "The effects of containment measures in the Italian outbreak of COVID-19"	Uses a time series approach
Timelli and Girardi (2021); "Effect of timing of implementation of containment measures on Covid-19 epidemic. The case of the first wave in Italy"	Only looks at timing
Trivedi and Das (2020); "Effect of the timing of stay-at-home orders on COVID-19 infections in the United States of America"	Only looks at timing
Umer and Khan (2020); "Evaluating the Effectiveness of Regional Lockdown Policies in the Containment of Covid-19: Evidence from Pakistan"	Too few observations
VoPham et al. (2020); "Effect of social distancing on COVID-19 incidence and mortality in the U.S."	Do not look at mortality
Wu and Wu (2020); "Stay-at-home and face mask policies intentions inconsistent with incidence and fatality during U.S. COVID-19 pandemic"	Too few observations
Xu et al. (2020); "Associations of Stay-at-Home Order and Face-Masking Recommendation with Trends in Daily New Cases and Deaths of Laboratory-Confirmed COVID-19 in	Do not look at mortality
Yehya, Venkataramani and Harhay (2020); "Statewide Interventions and Coronavirus Disease 2019 Mortality in the United States: An Observational Study"	Only looks at timing
Ylli et al. (2020); "The lower COVID-19 related mortality and incidence rates in Eastern European countries are associated with delayed start of community circulation Alban	Not effect of lockdowns

7.2 Interpretation of estimates and conversion to common estimates

In Table 9, we describe for each study used in the meta-analysis how we interpret their results and convert the estimates to our common estimate. Standard errors are converted such that the t-value, calculated based on common estimates and standard errors, is unchanged. When confidence intervals are reported rather than standard errors, we calculate standard errors using t-distribution with ∞ degrees of freedom (i.e. 1.96 for 95% confidence interval).

Table 9: Notes on studies included in the meta-analysis

1. Study (Author & title)	2. Date Published	3. Journal	4. Comments regarding meta-analysis
Alderman and Harjoto (2020); "COVID-19: U.S. shelter-in-place orders and demographic characteristics linked to cases, mortality, and recovery rates"	26-Nov-20	Transforming Government: People, Process and Policy	We use the 1% effect noted by the authors in "We find that the natural log of the duration (in days) that the state instituted shelter-in-place reduces percentages of mortality by 0.0001%, or approximately 1% of the means of percentages of deaths per capita in our sample. The standard error is calculated on basis of the t-value in Table 3.
Aparicio and Grossbard (2021); "Are Covid Fatalities in the U.S. Higher than in the EU, and If so, Why?"	16-Jan-21	Review of Economics of the Household	We use estimates from Table 3, model 5. For each estimate the common estimate is calculated as (difference in COVID-19 mortality with NPI)/(difference in COVID-19 mortality without NPI)-1, where (difference in COVID-19 mortality with NPI) is 237.89 (Table 2 states that deaths per million is 406.99 in U.S. and 169.10 in Europe) and (difference in COVID-19 mortality without NPI) is estimated as exp(ln(difference in COVID-19 mortality with NPI)-estimate).
Ashraf (2020); "Socioeconomic conditions, government interventions and health outcomes during COVID-19"	1-Jul-20	ResearchGate	It is unclear whether they prefer the model with or without the interaction term. In the meta-analysis, we use an average of -0.326 (Table 3, without) and -0.073 (Table 6, with) deaths per million per stringency point (i.e. -0.200). The common estimate is the average effect in Europe and United States respectively calculated as (Actual COVID-19 mortality) / (COVID-19 mortality with recommendation policy) -1, where (COVID-19 mortality with recommendation policy) is calculated as ((Actual COVID-19 mortality) - Estimate x Difference in stringency x population). Stringencies in Europe and United States are equal to the average stringency from March 16th to April 15th 2020 (76 and 74 respectively) and the stringency for the policy based solely on recommendations is 44 following Hale et al. (2020).

1. Study (Author & title)	2. Date Published	3. Journal	4. Comments regarding meta-analysis
Auger et al. (2020); "Association between statewide school closure and COVID-19 incidence and mortality in the U.S."	1-Sep-20	JAMA	Estimate that school closure was associated with a 58% decline in COVID-19 mortality and that the effect was largest in states with low cumulative incidence of COVID-19 at the time of school closure. States with the lowest incidence of COVID-19 had a −72% relative change in incidence compared with −49% for those states with the highest cumulative incidence.
Berry et al. (2021); "Evaluating the effects of shelter-in-place policies during the COVID-19 pandemic"	24-Feb-21	PNAS	The estimated effect of SIPO's, an increase in deaths by 0,654 per million after 14 days (significant, cf. Fig. 2), is converted to a relative effect on a state basis based on data from OurWorldInData. For states which did implement SIPO, we calculate the number of deaths without SIPO as the number of official COVID-19 deaths 14 days after SIPO was implemented minus 0,654 extra deaths per million. For states which did not implement SIPO, we calculate the number of deaths with SIPO as the number of official COVID-19 deaths 14 days after March 31 2020 plus 0,654 extra deaths per million. We use March 31 2020 as this was the average date on which SIPO was implemented in the 40 states which did implement SIPO. Using this approximation, the effect of SIPO's in the U.S. is 1,1% more deaths after 14 days. Common standard errors are not available.
Bjørnskov (2021a); "Did Lockdown Work? An Economist's Cross-Country Comparison"	29-Mar-21	CESifo Economic Studies	We use estimates from Table 2 (four weeks). Common estimate is calculated as the average of the effect in Europe and United States, where the effect for each is calculated as (ln(policy stringency) - ln(recommendation stringency)) x estimate.
Blanco et al. (2020); "Do Coronavirus Containment Measures Work? Worldwide Evidence"	1-Dec-20	World Bank Group	The study is not included in the meta-analysis, as it looks at the effect of NPIs on growth rates and does not include an estimate of the effect on total mortality.
Bonardi et al. (2020); "Fast and local: How did lockdown policies affect the spread and severity of the covid-19"	8-Jun-20	0	Find that, world-wide, internal NPIs have prevented about 650,000 deaths (3.11 deaths were prevented for each death that occurred, i.e. 76% effect). However, this effect is for any lockdown including a Swedish lockdown. They do not find an extra effect of stricter lockdowns and state that "our results point to the fact that people might adjust their behaviors quite significantly as partial measures are implemented, which might be enough to stop the spread of the virus." Hence, whether the baseline is Sweden, which implemented a ban on large gatherings early in the pandemic, or the baseline is "doing nothing" can affect the magnitude of the estimated impacts. Since all Western countries did something and estimates in other reviewed studies are relative to doing less – and, hence not to doing nothing, we report the result from Bonardi et al. as compared to "doing less." Hence, for Bonardi et al. we use 0% as the common estimate in the meta-analysis for each NPI (SIPO, regional lockdown, partial lockdown, and border closure (stage 1, stage 2 and full) because all NPIs are insignificant (compared to Sweden's "doing the least"-lockdown).
Bongaerts et al. (2021); "Closed for business: The mortality impact of business closures during the Covid-19 pandemic"	14-May-21	PLOS ONE	Business shutdown saved 9,439 Italian lives by 13th 2020. This corresponds to 32%, as there were 20,465 COVID-19-deaths in Italy by mid April 2020.
Chaudhry et al. (2020); "A country level analysis measuring the impact of government actions, country preparedness and socioeconomic factors on COVID-19 mortality and related health outcomes"	1-Aug-20	EClinacal-Medicine	Finds no effect of partial border closure, complete border closure, partial lockdown (physical distancing measures only), complete lockdown (enhanced containment measures including suspension of all non-essential services), and curfews. In the meta-analysis we use a common estimate of 0%, as estimates and standard errors are not available.
Chernozhukov et al. (2021); "Causal impact of masks, policies, behavior on early covid-19 pandemic in the U.S."	1-Jan-21	Journal of Econometrics	The study looks at the effect of NPIs on growth rates but does include an estimate of the effect on total mortality at the end of the study period for employee face masks (-34%), business closure (-29%). and SIPO (-18%), but not for school closures (which we therefore exclude). In reporting the results of their counterfactual, they alter between "fewer deaths with NPI" and "more deaths without NPI." We have converted the latter to the former as estimate/(1+estimate) so "without business closures deaths would be about 40% higher" corresponds to "with business closures deaths would be about 29% lower."
Chisadza et al. (2021); "Government Effectiveness and the COVID-19 Pandemic"	10-Mar-21	MDPI	The common estimate is the average effect in Europe and United States respectively calculated as (Actual COVID-19 mortality) / (COVID-19 mortality with recommendation policy) -1, where (COVID-19 mortality with recommendation policy) is calculated as ((Actual COVID-19 mortality) - Estimate x Difference in stringency x population). Stringencies in Europe and United States are equal to the average stringency from March 16th to April 15th 2020 (76 and 74 respectively) and the stringency for the policy based solely on recommendations is 44 following Hale et al. (2020). In the meta-analysis we use the non-linear estimate, but the squared estimate yields similar results.
Dave et al. (2021); "When Do Shelter-in-Place Orders	3-Aug-20	Economic Inpuiry	The study looks at the effect of SIPO's on growth rates but does include an estimate of the effect on total mortality after 20+ days for model 1 and 2 in Table 7. Since model 3, 4 and 5 have estimates

1. Study (Author & title)	2. Date Published	3. Journal	4. Comments regarding meta-analysis
Fight Covid-19 Best? Policy Heterogeneity Across States and Adoption Time"			similar to model 2, we use an average of model 1 to 5, where the estimates of model 3 to 5 are calculated as (common estimate model 2) / (estimate model 2) x estimate model 3/4/5.
Dergiades et al. (2020); "Effectiveness of government policies in response to the COVID-19 outbreak"	28-Aug-20	SSRN	The study is not included in the meta-analysis, as it looks at the effect of NPIs on growth rates and does not include an estimate of the effect on total mortality.
Fakir and Bharati (2021); "Pandemic catch-22: The role of mobility restrictions and institutional inequalities in halting the spread of COVID-19"	28-Jun-21	PLOS ONE	The study is not included in the meta-analysis, as it looks at the effect of NPIs on growth rates and does not include an estimate of the effect on total mortality.
Fowler et al. (2021); "Stay-at-home orders associate with subsequent decreases in COVID-19 cases and fatalities in the United States"	10-Jun-21	PLOS ONE	The study looks at the effect of SIPO's on growth rates but does include an estimate of the effect on total mortality after three weeks (35% reduction in deaths) which is used in the meta-analysis.
Fuller et al. (2021); "Mitigation Policies and COVID-19–Associated Mortality — 37 European Countries, January 23–June 30, 2020"	15-Jan-21	Morbidity and Mortality Weekly Report	For each 1-unit increase in OxCGRT stringency index, the cumulative mortality decreases by 0.55 deaths per 100,000. The common estimate is the average effect in Europe and United States respectively calculated as (Actual COVID-19 mortality) / (COVID-19 mortality with recommendation policy) -1, where (COVID-19 mortality with recommendation policy) is calculated as ((Actual COVID-19 mortality) - Estimate x Difference in stringency x population). Stringencies in Europe and United States are equal to the average stringency from March 16th to April 15th 2020 (76 and 74 respectively) and the stringency for the policy based solely on recommendations is 44 following Hale et al. (2020).
Gibson (2020); "Government mandated lockdowns do not reduce Covid-19 deaths: implications for evaluating the stringent New Zealand response"	18-Aug-20	New Zealand Economic Papers	We use the two graphs to the left in figure 3, where we extract the data from the rightmost datapoint (I.e. % impact of county lockdowns on Covid-19 deaths by 1/06/2020). We then take the average of the estimates found in the two graphs, because it is unclear which estimate the author prefers.
Goldstein et al. (2021); "Lockdown Fatigue: The Diminishing Effects of Quarantines on the Spread of COVID-19 "	4-Feb-21	CID Faculty Working	We convert the effect in Figure 4 after 90 days (log difference -1.16 of a standard deviation change) to deaths per million per stringency following footnote 3 (the footnote says "weekly deaths," but we believe this should be "daily deaths"), so the effect is e^-1.16 − 1 = −0.69 decline in daily deaths per million per SD. We convert to total effect by multiplying with 90 days and "per point" by dividing with SD = 22.3 (corresponding to the SD for the 147 countries with data before March 19, 2020 - using all data yields similar results) yielding -2.77 deaths per million per stringency point. The common estimate is the average effect in Europe and United States respectively calculated as (Actual COVID-19 mortality) / (COVID-19 mortality with recommendation policy) -1, where (COVID-19 mortality with recommendation policy) is calculated as ((Actual COVID-19 mortality) - Estimate x Difference in stringency x population). Stringencies in Europe and United States are equal to the average stringency from March 16th to April 15th 2020 (76 and 74 respectively) and the stringency for the policy based solely on recommendations is 44 following Hale et al. (2020).
Guo et al. (2021); "Mitigation Interventions in the United States: An Exploratory Investigation of Determinants and Impacts"	21-Sep-20	Research on Social Work Practice	We use estimates for "Proportion of Cumulative Deaths Over the Population" (per 10,000) in Table 3. We interpret this number as the change in cumulative deaths over the population in percent and is therefore the same as our common estimate.
Hale et al. (2020); "Global assessment of the relationship between government response measures and COVID-19 deaths"	6-Jul-20	medRxiv	The study is not included in the meta-analysis, as it looks at the effect of NPIs on growth rates and does not include an estimate of the effect on total mortality. They ascertain that "sustained over three months, this would correspond to a cumulative number of deaths 30% lower," however this is not a counterfactual estimate and three months goes beyond the period they have data for.
Hunter et al. (2021); "Impact of non-pharmaceutical interventions against COVID-19 in Europe: A quasi-experimental non-equivalent group and time-series"	15-Jul-21	Eurosurveillance	The study is not included in the meta-analysis, as they report the effect of NPIs in incident risk ratio which are not easily converted to relative effects.

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Langeland et al. (2021); "The Effect of State Level COVID-19 Stay-at-Home Orders on Death Rates"	5-Mar-21	Culture & Crisis Conference	The study is not included in the meta-analysis, as it looks at the effect of NPIs on odds-ratios and does not include an estimate of the effect on total mortality.
Leffler et al. (2020); "Association of country-wide coronavirus mortality with demographics, testing, lockdowns, and public wearing of masks"	26-Oct-20	ASTMH	Their "mask recommendation" includes some countries, where masks were mandated and may (partially) capture the effect of mask mandates. However, the authors' focus is on recommendation, so we do interpret their result as a voluntary effect - not an effect of mask mandate. Using estimates from Table 2 and assuming NPIs were implemented March 15 (8 weeks in total by end of study period), common estimates are calculated as 8^est-1.
Mccafferty and Ashley (2021); "Covid-19 Social Distancing Interventions by Statutory Mandate and Their Observational Correlation to Mortality in the United States and Europe"	27-Apr-21	Pragmatic and Observational Research	The study is not included in the meta-analysis, as it looks at the effect of NPIs on peak mortality and does not include an estimate of the effect on total mortality.
Pan et al. (2020); "Covid-19: Effectiveness of non-pharmaceutical interventions in the united states before phased removal of social distancing protections varies by region"	20-Aug-20	medRxiv	The study is not included in the meta-analysis, as the cluster the NPIs (e.g. SIPO, mask mandata amd travel restricions are clustered in Level 4).
Pincombe et al. (2021); "The effectiveness of national-level containment and closure policies across income levels during the COVID-19 pandemic: an analysis of 113 countries"	4-May-21	Health Policy and Planning	Policy implementations were assigned according to the first day that a country received a policy stringency rating above 0 in the OxCGRT stay-at-home measure. As the value 1 is a recommendation "recommend not leaving house," we cannot distinguish recommendations from mandates, and, thus, the study is not included in the meta-analysis.
Sears et al. (2020); "Are we #stayinghome to Flatten the Curve?"	6-Aug-20	medRxiv	Find that SIPOs lower mortality by 29-35%. We use the average (32%) as our common estimate. Common standard errors are calculated based on estimates and standard errors from (Table 4) assuming they are linearly related to estimates.
Shiva and Molana (2021); "The Luxury of Lockdown"	9-Apr-21	The European Journal of Develepment Research	The estimate with 8 weeks lag is insignificant, and preferable given our empirical strategy. However, they use the 4-week lag when elaborating the model to differentiate between high- and low-income countries, so the 4-week lag estimate for rich countries is used in our meta-analysis. Common estimate is calculated as the average of the effect in Europe and United States, where the effect for each is calculated as (policy stringency - recommendation stringency) x estimate.
Spiegel and Tookes (2021); "Business restrictions and Covid-19 fatalities"	18-Jun-21	The Review of Financial Studies	We use weighted average of estimates for Table 4, 6, and 9. Since authors state that they place more weight on the findings in Table 9, Table 9 weights by 50% while Table 4 and 6 weights by 25%. We estimate the effect on total mortality from effect on growth rates based on authors calculation showing that estimates of -0.049 and -0.060 reduces new deaths by 12.5% 15.3% respectively. We use the same relative factor on other estimates.
Stockenhuber (2020); "Did We Respond Quickly Enough? How Policy-Implementation Speed in Response to COVID-19 Affects the Number of Fatal Cases in Europe"	10-Nov-20	World Medical & Health Policy	When calculating arithmetic average / median, the study is included as 0%, because estimates in Table 6 are insignificant and signs of estimates are mixed (higher strictness can cause both fewer and more deaths). We don't calculate common standard errors.
Stokes et al. (2020); "The relative effects of non-pharmaceutical interventions on early Covid-19 mortality: natural experiment in 130 countries"	6-Oct-20	medRxiv	We use estimates from regression on strictness alone (Right panel in Table "Regression results, policy strictness. Baseline is "policy not introduced within policy analysis period" in "Additional file"). We use the average of 24 and 38 days from model 5. There are 23 relevant estimates in total (they analyze all levels within the eight NPI measures in the OxCGRT stringency index). We calculate the effect of each NPI (e.g. closing schools) as the average effect in all of U.S./Europe. This is done by calculating the effect for each state/country based on the maximum level for each measure between Mar 16 and Apr 15 (e.g. if all schools in a state/country are required to close (school closing level 3) the relevant estimate for that state/level is -0.031 (average of -0.464 and 0.402). We assume all NPIs are effective for 54 days (from March 15 to June 1 minus 24 days to reach full effect). Standard errors are converted to common standard errors following the same process (this approach is unique for Stokes, as our general approach is not possible).

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Toya and Skidmore (2020); "A Cross-Country Analysis of the Determinants of Covid-19 Fatalities"	1-Apr-20	CESifo Working Papers	It is unclear how they define "lockdown." They write that "many countries [...] imposed lockdowns of varying degrees, some imposing mandatory nationwide lockdowns, restricting economic and social activity deemed to be non-essential," and since all European countries and all states in the U.S. imposed restrictions on economic (closing unessential businesses) and/or social (limiting large gatherings) activity, we interpret this as all European countries and all U.S. states had mandatory nationwide lockdowns. The effect of recommended lockdowns is set to zero in the meta-analysis, as only one country was in this lockdown category (i.e. too few observations, cf. eligibility criteria). The estimate for complete travel closure is -0.226 COVID-deaths per 100,000. Hence, if all of Europe imposed complete travel closure, the total effect would be -0.266 * 748 million (population) * 10 (100,000/1,000,000) equal to 1,690 averted COVID-19 deaths. However, according to OxCGRT-data European countries only had complete travel bans (Level 4: "Ban on all regions or total border closure") in 11% of the time between March 16 and April 15, 2020. So the total effect is 1,690 * 11% = 194 averted deaths. During the first wave 188,000 deaths in Europe was related to COVID-19 (by June 30, 2020), so the total effect is approximated to -0.1% in Europe and, following the same logic, 0% in U.S., where no states closed their borders completely. We use the average, -0.05%, in the meta-analysis. The estimate for mandatory national lockdown is 0.166 (>0) COVID-deaths per 100,000. Since all European countries (and U.S. states) imposed lockdowns, the total effect is 1,241 (553) extra COVID-19 deaths corresponding to 0.7% (0.4%). We use the average of Europe and the U.S., 0.5%, in the meta-analysis. Calculations of the effect of "Mandatory national lockdown" follow the same logic, but we assume 100% of Europe and United States have had "Mandatory national lockdown."
Tsai et al. (2021); "Coronavirus Disease 2019 (COVID-19) Transmission in the United States Before Versus After Relaxation of Statewide Social Distancing Measures"	3-Oct-20	Oxford academic	The study is not included in the meta-analysis, as they report the effect of NPIs on Rt which are not easily converted to relative effects.

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PRODUKTIE 8

Aggressive Measures, Rising Inequalities and Mass Formation During the COVID-19 Crisis: An Overview and Proposed Way Forward

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Abstract

A series of aggressive restrictive measures around the world were adopted in 2020-2022 to attempt to prevent SARS-CoV-2 from spreading. However, it has become increasingly clear that an important negative side-effect of the most aggressive (lockdown) response strategies may involve a steep increase in poverty, hunger, and inequalities. Several economic, educational and health repercussions have not only fallen disproportionately on children, students, and young workers, but also and especially so on low-income families, ethnic minorities, and women, exacerbating existing inequalities. For several groups with pre-existing inequalities (gender, socio-economic and racial), the inequality gaps widened. Educational and financial security decreased, while domestic violence surged. Dysfunctional families were forced to spend more time with each other, and there has been growing unemployment and loss of purpose in life. This has led to a vicious cycle of rising inequalities and health issues. In the current narrative review, we describe macro-dynamics that are taking place as a result of aggressive public health policies and psychological tactics to influence public behavior, such as mass formation and crowd behavior. Coupled with the effect of inequalities, we describe how these factors can interact towards aggravating ripple effects. In light of evidence regarding the health, economic and social costs, that likely far outweigh potential benefits, the authors suggest that, first, where applicable, aggressive lockdown policies should be reversed and their re-adoption in the future should be avoided. If measures are needed, these should be non-disruptive. Second, it is important to assess dispassionately the damage done by aggressive measures and offer ways to alleviate the burden and long-term effects. Third, the structures in place that have led to counterproductive policies, should be assessed and ways should be sought to optimize decision-making, such as counteracting groupthink and increasing the level of reflexivity. Finally, a package of scalable positive psychology interventions is suggested to counteract the damage done and improve future prospects for humanity.

1 Introduction

Historically, health crises have prompted governments and other authorities to act, with differing outcomes (cf. Adler et al., 2022; Biesma et al., 2009; Jedwab et al., 2021). Global and local health initiatives have long been in place (e.g., see WHO, 2018). For the COVID19 crisis, governments, and other authorities (e.g., public health agencies, state and county leaders for their citizens, or businesses for their employees) adopted different ways of dealing with the crisis around the world. A key ingredient of their response often included restrictive population-wide measures, summarily called here non-pharmaceutical interventions (NPIs). When studying the effects of the health policies employed, three findings become apparent: (1) there is little proof that most aggressive measures work much better than less disruptive, focused measures (e.g., Fögen, 2022; Guerra & Guerra, 2021; A. R. Joffe & D. Redman, 2021) for reducing COVID-19 burden; (2) some adopted measures may even have severe negative consequences (for reviews see e.g., Joffe & Redman, 2021; Panneer et al., 2022; Schippers, 2020) and (3) decision-makers have overly focused on one problem, COVID-19, at the expense of taking a more holistic approach (Joffe, 2021; Melnick & Ioannidis, 2020; Schippers & Rus, 2021). Together, this crisis management has led to rising inequalities and created new ones (Aspachs et al., 2021; Binns & Low, 2021). For instance job and food insecurity rose sharply during the crisis due to the global response (Spring et al., 2022). Some scientists have even concluded that lockdowns may be the "single biggest public health mistake in history" (Bhattacharya, 2021; Marmalejo, 2022), worrying that negative effects may be felt for years to come (Hevia & Neumeyer, 2020; Schippers, 2020).

Despite this, many countries opted for long-term strict and aggressive NPIs (Kraaijeveld, 2021). A recent review and meta-analysis concluded that while lockdowns had little or no beneficial health effects, the economic and social costs were huge (Herby et al., 2022). Measures such as closing restaurants and businesses and disrupting global supply chains (Chowdhury et al., 2021; Guan et al., 2020; Singh et al., 2021) have taken a toll on the world economy, and on physical and mental health (Santomauro et al., 2021; Schippers, 2020; Taquet et al., 2021). As early as November 2020, an article published by the World Bank estimated that the COVID-19 crisis would push between 88 and 115 million people into extreme poverty (Yonzan et al., 2020), and a sharp increase in food insecurity worldwide led to hundreds of millions of additional people at risk of starving and even more people becoming food-insecure (Paslakis et al., 2020; Zetzsche, 2020; Oxfam, 2021; Nelson et al., 2021). These macro-economic

consequences can lead to a steep increase in mental health issues (Jones, 2017; Nanath et al., 2022) and even fragmentation of society (Storm, 2021). Aggressive health policies may have long-term negative economic and health consequences especially if they are related to increasing inequalities (Wachtler et al., 2020). For instance, children who experience food insecurity early in life, may develop poor eating pathologies later on in life (Paslakis et al., 2020). Wealth distributions have become more skewed, worsening a pre-pandemic-crisis. The top 10% of the global population owns 76% of the total wealth, while the bottom 50% share a mere 2% (Civilsdaily, 2021). In September 2021, just over one percent of the world's population held 45.8% of global wealth (Deshmukh, 2021).

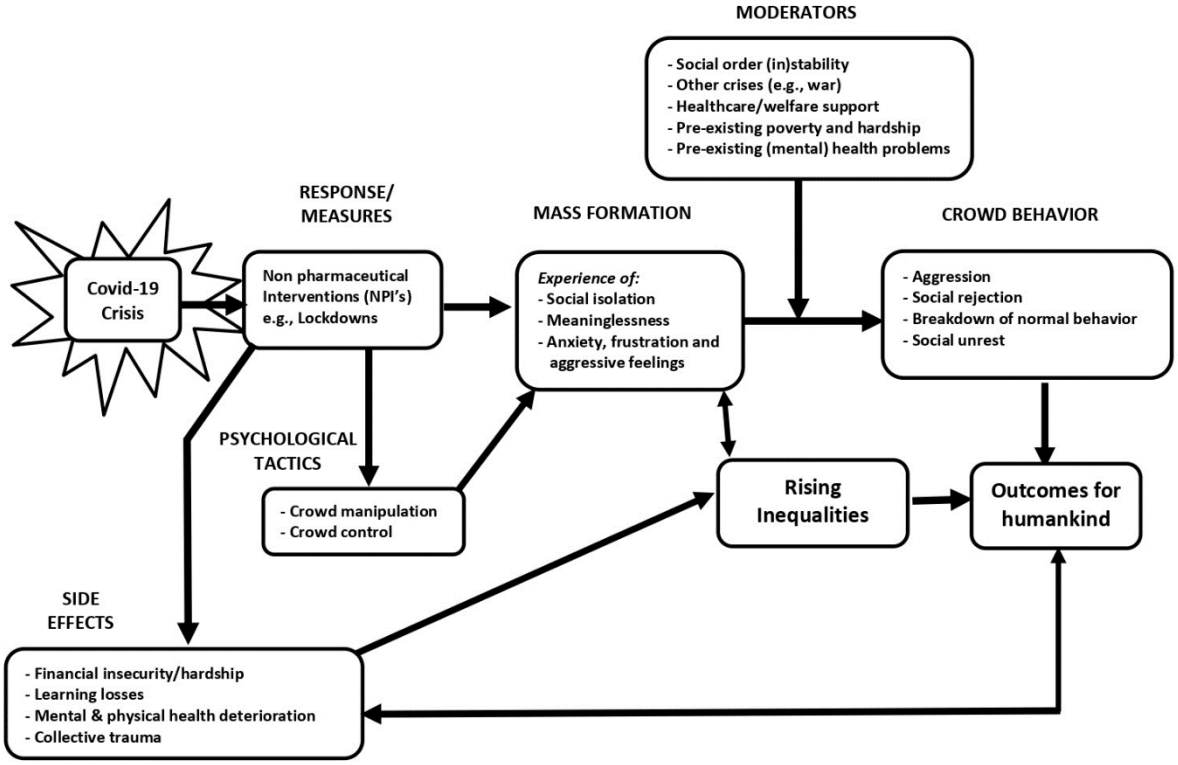
Prior research has shown that, both in the animal kingdom, and within the human population, (extreme) levels of inequality often give rise to hierarchies and status dynamics that lead to negative health outcomes (Calhoun, 1973; Sapolsky, 2005; Sapolsky & RI, 2004; Smith et al., 1990; Snyder-Mackler et al., 2020). The Whitehall studies investigating long-term social determinants of health, found higher mortality rates from men and women of lower employment grade, compared to individuals in higher employment grade and status (Chen & Miller, 2013). Up to twenty years of difference in life expectancy has been observed between countries with large status and economic differences versus more well-off egalitarian countries (Marmot & Wilkinson, 2005). Some NPIs may have a large effect on increasing pre-existing inequalities and creating new ones, posing a threat to health and increasing mortality and shortening longevity (Binns & Low, 2021). Some behavioral interventions along with NPIs used by governments to enforce compliance, also worsened inequality. Concurrently, the COVID-19 crisis and the measures taken seem to have offered an opportunity to well-off people who profited from the transformation of life from physical to digital (e.g., Bajos et al. 2021), and/or profited financially from the crisis (Plott et al., 2020). Many large companies profited, while many small companies crumbled, accelerating pre-existing trends (Baines & Hager, 2021).

Taken together, the rising inequalities are related to consequences beyond mere financial insecurity, given the dynamism of extreme hierarchical differences (Kira et al., 2021). From a macro-dynamic perspective, aggressive health policies accompanied with psychological tactics to influence public behaviour, have consequences such as mass formation and crowd behavior (i.e. the influence that large groups have on individual behaviour), and breakdown of normal behavior (cf. de Jong et al., 2020; Desmet, 2022). The burden of harmful side effects, such as

financial and food insecurity for billions of people, accompanied with a deterioration of mental and physical health falls disproportionally on already disadvantaged groups (Cheng et al., 2021; Krauss et al., 2022), with predictable consequences for social capital and health (Corman et al., 2012; Dickerson et al., 2022; Polsky & Gilmour, 2020). The general insecurity and trauma caused by the insecurity and uncontrollability of the events also contribute to mental health issues (de Jong et al., 2020; Dickerson et al., 2022; Vermote et al., 2022). While for some NPIs, the negative effects could have been foreseen, judging from the reports and information that were already available (e.g., WHO, 2018), it may also make sense to assess in hindsight what went wrong in both the decision-making process and crisis management and what lessons for the future can be learned.

In the current narrative review, we first aim to elucidate mechanisms that explain the potential harmful effects of aggressive NPIs (e.g., financial and food insecurity, learning losses and deterioration in mental and physical health; See Figure 1). We describe how these NPIs impact mass formation and crowd behavior, via psychological tactics such as crowd manipulation and control. We describe how these affect inequalities and in turn outcomes for humankind. We then review the literature and describe the effects of NPIs and mandates on different groups in society and the resulting increase in inequalities. We offer a non-exhaustive overview of the effects on inequalities resulting from the pandemic and NPIs. These include socio-economic, gender, (mental and physical) health, and educational inequalities, as well as the rising inequalities for many ethnic groups. We end with a discussion and recommendations on ways to mitigate the negative effects resulting from aggressive measures.

Figure 1. Theoretical model of the consequences of the NPI's on rising inequalities and outcomes for humankind



2 Aggressive Measures, Mass Formation and Crowd Behavior

During the COVID-19 crisis, governments took the lead in managing the crisis. They relied on NPIs to manage the crisis. However, in 2007 and in 2019 reports concluded that high-quality research on NPIs is lacking, and a list of NPIs was assessed in terms of effectiveness (Aledort et al., 2007; WHO, 2019). In the 2007 paper, it was commented that the scientific base of high quality studies on NPIs is exceeding small (Aledort et al., 2007), and interventions that were explicitly *not* recommended were the general use of masks and other protective equipment and social distancing (Aledort et al., 2007). Also, the experts surveyed for this research mentioned that forcibly limiting assembly or movement was legally and ethically problematic; they thought that mandatory long-term community restrictions and compulsory quarantine would lead to public opposition, practical and logistical problems. It was concluded that voluntary measures and guidelines would be more acceptable and thus effective (Aledort et al., 2007). The 2019 WHO report speaks of spreading cases over a longer period of time in order to reduce the height of the peak in "cases" but mentions NPIs such as community use of face masks,

border closures, entry- and exit screening and school closures as generally ineffective. Of the 18 NPIs mentioned in the report, measures such as ventilation and isolation of sick individuals were seen as effective (WHO, 2019). The quality of the most studies was rated as (very) low, making it hard to determine effective NPIs, and the possible harmful effects were not weighed. In 2020, a WHO report appeared with considerations on how to ease measures and this report also discussed the importance of human rights protection and protection of vulnerable populations (WHO, 2020). The extent to which governmental decision-making was flawed is still a matter of debate (e.g., J. P. A. Ioannidis, 2020).

Several social psychological theories can explain what could have gone wrong in terms of these interactions. Group processes and crowd psychology predicts that especially in times of crisis people will be inclined to look at governments and authorities to guide their behavior (cf. Adler et al., 2022; Jedwab et al., 2021). As these authorities respond with guidelines for behavior and NPIs, this can lead to mass formation and crowd formation, similar to the way molecules behave or swarms, with ensuing collective behavior (Desmet, 2022; Edmonds, 2006; Le Bon, 2002). Members of such groups often develop a high degree of emotional like-mindedness, and conventional inhibitions are often not apparent in such groups (Kok et al., 2016). In light of the crisis, experts were asked to advise governments and these used behavioral interventions to steer public behavior in the desired direction and at the same time the debate became highly polarized and politicized (Bor et al., 2022; Bylund & Packard, 2021). Indeed, the behavior of people changed quite radically in the early days of the crisis (Drury et al., 2021; Prentice et al., 2022), as psychologists advised governments on how to use psychological tactics to affect behavior change (e.g., Bavel et al., 2020a; Rayamajhee & Paniagua, 2022). A special journal issue described the many social group psychological aspects such as impact on societies, social connectedness and new collective behaviors and inequalities (Krings et al., 2021). Within the social psychological field of crowd psychology, explanations are offered as to why the behavior of a crowd differs from that of the individuals within the crowd. These theories view the crowd as an entity, where individual responsibility is lost (Le Bon, 2018). In such a crowd, individuals tend to follow predominant ideas and emotions of the crowd, in a form of shared consciousness, or “collective mind”. Then it becomes relatively easy to violate personal and social norms and such crowds can become destructive (Le Bon, 2002). This theory may help explain deindividuation and aggression sometimes seen in large groups (Postmes & Spears, 1998). In such groups, deindividuated people often show more sensitivity and conformance to situation-

specific norms and support a social identity model of deindividuation (Postmes & Spears, 1998).

In the early phase of a crisis, people are inclined to embrace a superordinate level of identity and look for (national) leaders for support and guidance (Abrams, Lalot, et al., 2021). Strong responses towards group members who deviate from new norms are deemed legitimate by many (Abrams, Lalot, et al., 2021; Abrams, Travaglino, et al., 2021), although this may also be dependent on the status of the group member (Wiggins et al., 1965), and can change as the crisis progresses. Fluctuations or changes in group behaviors occur later on as people's expectations of a return to normalcy are not met, or if they realize the downsides (Abrams, Lalot, et al., 2021). Indeed, as discontent rises around the globe, citizens may engage in activism (Grant & Smith, 2021) as well as lawsuits against authorities for what in their view is poor crisis management (Sharp, 2010). In times of crisis, , blame is often laid on minority groups, who are subsequently scapegoated and persecuted (Jedwab et al., 2021). This effect adds to minorities and poorest already carry the largest burden for the NPIs (Chirisa et al., 2022; Schippers, 2020; Spring et al., 2022).

3 Psychological tactics

3.1 Crowd manipulation, propaganda, crowd control

As people turn to leaders in times of crisis (Mayseless & Popper, 2007; Volkan, 2014), leaders have an important responsibility to make important and consequential decisions (Schippers & Rus, 2021). These leaders can choose to intervene in different ways. In general, and especially at the beginning of a crisis, people are inclined to ask for and accept strong leadership (cf. Antonakis, 2021; Binagwaho, 2020). Leaders faced the choice between espousing voluntariness in policies or mandating rules and regulations to deal with the crisis (Gupta et al., 2020; Schmelz & Bowles, 2022; Yan et al., 2021). Although during crisis, leaders have a tendency to enforce rules (Teichman & Underhill, 2021), some voluntariness may be key to trust in government (Schmelz, 2021). There is some evidence that support for the measures will be greater under voluntary than under enforced implementation (Schmelz, 2021), and that voluntariness may offset the experienced disadvantages of policies (Kraaijeveld, 2021; Yan et al., 2021). In general, citizen engagement has many advantages (Carpini et al., 2004). Moreover, it seems that many assumptions on which the NPIs are founded, seem to be biased

at best (Ioannidis, 2020; Schippers, 2020; Schippers & Rus, 2021). A review of over 100 studies about the COVID-19 crisis handling revealed that many studies relied on false assumptions and overall, the net effects of the policies were negative (Allen, 2022). Furthermore, it was shown that lockdowns were very costly economically, but probably did not save lives (Gibson, 2022; Joffe & Redman, 2021). Other options such as involving communities in responses to collective threats, may have avoided many if not all of the negative side effects (Drury et al., 2021), and voluntary measures may have been better in terms of ethics and human rights (Kraaijeveld, 2021; Silverman et al., 2020).

Crowd manipulation, or the use of behavior change techniques based on crowd psychology, could have both intended and unintended consequences (Desmet, 2022). While the theory of mass formation has been criticized for being too general (McPhail, 2017), it is a meta-theory that seems to be supported by more micro- and middle-range theories on the social psychology of group dynamics and group behavior. These include theories such as group cohesion and intergroup conflict (Desmet, 2022). For instance, large increases in perceived threat to a group were significantly related to diminished problem-solving effectiveness (Rempel & Fisher, 1997). A meta-analysis studying 335 effect sizes from 83 samples across 31 countries found that under conditions of strong population norms, norm-behavior associations were also stronger (i.e. people acting according to their norms), and the level of collectivism strengthened these norm effects (Fischer & Karl, 2022). Governments around the world have strongly communicated a high level of threat and called on norms of collectivism, obedience and solidarity to excuse NPIs and accompanying harms (Schippers, 2020). While these manipulations can in theory benefit the public, the required behaviors have had harmful consequences, ever more so for already vulnerable groups (Herby et al., 2022; Schippers, 2020; Schippers & Rus, 2021). Note that one does not need to invoke some nefarious totalitarianism (Arendt, 1973). There can be extreme bonding among people in order to defeat a real or imagined enemy, in this case a virus (Abrams, Lalot, et al., 2021). A meta-analysis showed that there is a tendency of ingroup bonding (closing the ranks) combined with a tendency to focus on the outgroup as the source of the threat (Riek et al., 2006). Even when external threats are not related to a specific outgroup, hostility, prejudice and discrimination are aimed at outgroups, and detrimental intergroup outcomes occur (Adler et al., 2022). Dehumanization, or the “act of denying outgroup members human-like attributes” (Adler et al., 2022, p. 110) may be a mediating factor between a perceived threat and negative behaviors and attitudes

toward that group (Haslam & Stratemeyer, 2016). For COVID-19 crisis, the superimposed economic crisis contributes to higher levels of hostility and discrimination (and dehumanization) of outgroups to which the cause of the crisis is attributed (Adler et al., 2022; Becker et al., 2011; Fritsche et al., 2011; Krosch et al., 2017). Interestingly, this prejudice against outgroups was not apparent when a system-level explanation for a crisis, i.e. the economic system, was made salient (Becker et al., 2011). Also, the status of the outgroup moderates this effect: the prejudice is lower when the status of the outgroup is higher (Riek et al., 2006).

Mass formation with respect to reacting to an external threat combined with the resulting extreme inequality, can potentially be very harmful (cf. Becker et al., 2011; Krosch et al., 2017). Citizen behavior may be unfortunately steered into a direction of societal damage. Mass formation can make people adopt ideas that are incompatible with their previous beliefs. For instance, many people with supposedly progressive ideologies supported harsh measures against unvaccinated people, such as requiring unvaccinated individuals to always remain confined to their homes. Some thought governments should even imprison individuals who publicly questioned vaccine risk-benefit. Moreover, they also thought that unvaccinated individuals should have a tracking device, or be locked up in designated facilities or locations until they are vaccinated (Shannon, 2022). These beliefs have nothing to do with improving the uptake of effective vaccines (a most welcome outcome) but delve into other priorities where aggression is the main theme. This kind of dehumanization of a large group could create a whole new kind of inequality: a privileged group of people religiously following governmental response versus a scapegoated group questioning official policies.

The divide between those groups may have many consequences, from not being willing to work with a co-worker who fails to conform, to condoning the violation of basic human rights for such a group with exclusion from society (Bor et al., 2022). A bias seems to work in the direction of the government responses: a study using a representative sample from 10,270 respondents from 21 countries showed that vaccinated people have high antipathy against unvaccinated people, 2.5 times more than a more traditional target such as immigrants from the Middle East (Bor et al., 2022). Interestingly, the antipathy is larger in countries with higher social trust and fewer COVID-19 deaths. In the study, no bias from the unvaccinated towards the vaccinated was detected (Bor et al., 2022). Why would otherwise agreeable and average people hold such beliefs? The answer may be that redirecting the blame towards a scapegoat

may help people restore a sense of control, easing feelings of uncertainty (Sullivan et al., 2010). For instance, participants "were especially likely to attribute influence over life events to an enemy when the broader social system appeared disordered" (Sullivan et al., 2010; Study 3). The consequences of crowd behaviors like dehumanization and scapegoating in general may be quite severe, and it would be advised to work towards reducing intergroup tensions instead of fueling them (Adler et al., 2022). However, many government responses may have increased these effects rather than reduced them. For political reasons, sometimes governments chose to attribute the blame to some "enemy" while presenting themselves as the savior (Jedwab et al., 2021; Petersson, 2009). For the general public, in addition to a social and economic divide, these NPIs and such framing of the message can lead to feelings of social isolation, loss of meaning in life, anxiety and aggressive feelings (Desmet, 2022).

3.2 Experience of Social isolation, Meaninglessness, Anxiety, Frustration and Aggressive Feelings

The COVID-19 crisis, as with any crisis, spurs feelings of anxiety, frustration and aggression (Slavich, 2022). Social safety theory would predict that social threat greatly impacts human health and behavior (Slavich, 2022). Social isolation has led to the experience of meaninglessness, although the role of mindsets about the COVID-19 situation has been important (Zion et al., 2022). Three mindsets that people formed early in the pandemic, namely considering the pandemic as a catastrophe, as manageable or as an opportunity, had a self-fulfilling impact on emotions, health behaviors, and wellbeing (Zion et al., 2022). In general, the heightened level of mortality salience has been related to heightened frustration and aggression in society (cf. Slavich, 2022) and especially aggression towards those with opposing world views (Pyszczynski et al., 2021). Human aggression refers to intentional harmful behaviors directed at other individuals, and violence is aggression that has extreme harm as a goal. Hostile aggression is seen as a form of aggression that is rather impulsive or unplanned, while instrumental aggression is premeditated and a proactive form of aggression that is used as a means to an end (for a review see Anderson & Bushman, 2002). Aggressive thoughts and feelings are probably even more common, as many situations and interactions with others can give rise to frustration and aggression. While pre-existing biological and learned tendencies may play a role, the current situation gives rise to a spike in aggressiveness, both in words (e.g., people blaming certain groups for the current situation and thinking aloud about what should happen to such groups), as well as in actual aggression. There is some evidence that

interpersonal aggression and violence increased with aggressive NPIs, especially in places with lockdowns and stay-at-home orders (Killgore et al., 2021; Mazza et al., 2020). As the crisis continued for much longer than initially expected, aggression and frustration could accumulate, without people having many chances to vent, e.g., by going to the gym.

Excitation transfer theory can explain why anger may be extended over longer periods of time, and this often happens when two or more arousing events are close in terms of time (Zilman, 1983). When people are in a survival mode for prolonged periods of time, they become more fearful, distrustful, irritable and aggressive (Bezo & Maggi, 2015). Although a survival mode can be an adaptive response to an immediate threat or existential danger, in the long-run over-exposure of stress-response hormones harms mental health and relationships and leads to intergenerational trauma (Bezo & Maggi, 2015; Brom, 2014). Displaced aggression directed at another person or target, that is not the source of the arousing frustration, can also occur. A meta-analysis showed that the magnitude of the displaced aggression was bigger in a negative setting (e.g., the current crisis). Also, if the provocateur and target were more similar to each other e.g., in terms of gender, race, and/or values, displaced aggression was higher (Marcus-Newhall et al., 2000).

A study among 2,799 Chinese college students (Ye et al., 2021) showed that the relationship between fear of COVID-19 and relational online aggressive behavior is mediated by moral disengagement (i.e. the process by which people convince themselves that ethical standards do not apply to them in a certain context, by reframing their behavior as morally acceptable). High mortality salience can also increase aggression, often directed at others who threaten one's world-view (McGregor et al., 1998). Note that terror management can also lead to a more positive way of coping, such as reflecting on the meaning of life (Pyszczynski et al., 2021), and this may be a more effective way of dealing with crisis (de Jong et al., 2020). However, a study among 1,374 participants in seven Arab countries showed that traumatic stress coupled with collective identity trauma increased death anxiety. This was in turn related to reduced well-being, post-traumatic stress syndrome, anxiety and depression (Kira et al., 2021). The authors speak of a vicious cycle of inequalities increasing infection and death from COVID-19 and the COVID-19 crisis increasing inequalities further (Kira et al., 2021). As many of the behaviors aimed at reducing the spread of the virus, such as hand-washing or masking, can be seen as group rituals (i.e. acts that people regularly repeat together in the same way), symbolizing important group values (e.g., health and safety) people deviating from such rituals

provoke anger and moral outrage (Stein et al., 2021; Schippers, 2020).Individuals more worried of contracting the disease made harsher moral judgments than less worried individuals, even after controlling for political orientation (Henderson & Schnall, 2021).

There is also evidence that the COVID-19 crisis has increased psychological distress that could be related to proximal and distal defences against death-related thoughts (Kira et al., 2021). The crisis has increased anxiety and fear for personal and loved one's physical well-being (Lathabhavan & Vispute, 2021). Conversely, physical activity could act as a buffer (Wright et al., 2021) but the anxiety-buffering outlets such as a social network and sports were inaccessible for many, leaving people vulnerable to experiencing even higher levels of death anxiety (Kira et al., 2021; Pyszczynski et al., 2021). A "perfect storm" ensued, whereby stress and anxiety increased and pathways for releasing stress were cut off for many. Furthermore, all of the social determinants of health were affected; none of these was equally distributed even before the crisis started, but the crisis has accelerated this uneven distribution (Alamilla & Cano, 2022; Bambra et al., 2021). Much of these effects have been a result of government response to the crisis and the choices made in this respect (Bambra et al., 2021). In many countries, decisions were made unilaterally and an official narrative was supported and defended (Idler et al., 2022).

4 Centralized decision making and one narrative

Decision making during a health crisis is difficult as many issues need to be considered concurrently with an input from data that may be lacking or massive but still flawed (Khoury & Ioannidis, 2014; Schippers & Rus, 2021). Collective decision-making and intelligence are key to effective decision-making (Kameda et al., 2022). However, sometimes it is falsely assumed that in a major crisis centralized decision making is the only method that may work. Another potential bias may be that a small group of experts is listened to, at the expense of experts that advocate a different route to solve the crisis (Hughes et al., 2021). An official narrative approach was followed (Idler et al., 2022; Pleyers, 2020), and counter narratives routinely labelled as misinformation (Greer et al., 2022). Sometimes the experts in control acquire so much power that they take over even the role of the opposition and dissenters are ostracized (Godlee, 2021; Kaufmann, 2021; Sunstein, 2005). In the current crisis, authorities have used media and public communication to impose their narrative (Pleyers, 2020). People and groups challenging the narrative often face dire consequences, from social exclusion to

arrest and molestation at demonstrations, in both authoritarian and democratic countries (Pleyers, 2020). Concurrently, the question has been raised if coercive measures are desirable policy responses, as these have been seen as ineffective and counterproductive in the past (Kavanagh & Singh, 2020), leading to distrust in institutions, alienating communities and avoidance of care (Gostin & Hodge, 2020; National Academy of Medicine et al., 2007; WHO, 2016; Kavanagh & Singh, 2020). The combination of coercive measures and a cancel culture to preserve an official narrative may lead to a backlash or even boomerang effect in the longer term (Kavanagh & Singh, 2020; Sly, 2020). Public persuasive communication backfires and may lead to the opposite effect or behavior than intended (Byrne & Hart, 2009; Cohen, 1962).

Historically, mixing political ideology with science, when the state basically regulates science, has led to disastrous outcomes. For instance, in the former Soviet Union, a geneticist favored by Stalin, dominated biology and agricultural science, rejecting Mendelian genetics. The careers and lives of geneticists who opposed him were destroyed, many of them arrested or killed (Kean, 2017; Kolchinsky et al., 2017). This one-sided approach led to mass starvation in Russia and also, when the Chinese Communists adopted the same approach, starvation killed 30 million people (Kean, 2017). Favoring one ideology at the expense of other views limits academic freedom and can lead to unwanted outcomes (Joffe, 2021; Rittberger & Richardson, 2019; Schippers, 2020; Schippers & Rus, 2021), where ironically sometimes free speech is used to shut down free speech (Motta, 2018; Teixeira da Silva, 2021). The resulting "cancel culture" may frighten other academics who will then be careful in speaking out and/or publishing on certain topics (Rittberger & Richardson, 2019) Extreme centralized decision making has other disadvantages, including diminishing democracy, diminished freedoms, and threats to human rights (Della Porta, 2020a; Ioannidis & Schippers, 2022; Daly, 2022; Della Porta, 2020b; Seedhouse, 2020). Trust in government may diminish, and support for the NPIs may waver (Schmelz, 2021). While COVID-19 was a major problem, tackling it should never be done to the exclusion of all other problems we face as humanity (J. P. Ioannidis, 2020). Making decisions should preferably be done in a way that serves most humans, and science can aid here, but it should not be pretended that "science" is leading decision-making or that it is perfect and error-free (cf. (Ioannidis, 2005). Concurrently, journalism and science should be investigative and open-minded instead of blindly following one narrative and thus becoming a tool for propaganda (Seedhouse, 2020). The result may have been suboptimal decision-making (Schippers & Rus, 2021), people feeling helpless and losing their goal in life (de Jong et al., 2020), and a range of negative economic and health ripple effects (see Figure 1).

4.1 Counter movement

Grassroots movements and counter movements have gained more research attention lately (Carty, 2010; Carty & Onyett, 2006; Fournier, 2002; Goodwin et al., 2006; Gulliver et al., 2021; Roy, 2021). As the distribution of power has been unequal throughout history, and is typically held by an elite minority, enabling people to use collective power is an important aim of those movements (Moyer et al., 2001). The elite may be inclined to benefit itself at the expense of general welfare (Moyer et al., 2001). A struggle ensues between vested interests and a movement aiming for social change and justice (Moyer et al., 2001). Power in this respect equals controlling resources, knowledge and even attempts to control what people think, and different tactics such as persuasion, persecution, coercion, propaganda, and even physical violence are often used to control behavior (Moyer et al., 2001). This may cause a sharp decrease in trust in institutions for some, while other people keep being trustful and believe the elite has their best interest at heart. With the COVID-19 crisis, trust in governments and scientific institutions oscillated but mostly decreased (Hamilton & Safford, 2021). Often, a trigger event and (non-violent) action campaigns alert the general public, often leading to outrage, especially when there is perceived contradiction between widely held values and principles and the actual policies and behaviors of those in power (Moyer et al., 2001). Many people may join counter movements because they give meaning as well as an opportunity to act upon and reinstate dearly held values and beliefs (Sovacool & Dunlap, 2022). Many citizen activists feel they contribute to a better world in this way; especially the younger generation may be driven more by moral issues rather than by more traditional ideologically oriented political structures (Müller-Bachmann et al., 2022). The will to act is dependent on macrosocial structural conditions, imaginations of the future with regard to alternative possibilities, and the level of self-efficacy in engendering social change (Müller-Bachmann et al., 2022). These movements often rely on self-organizing communities, that organize activities such as social and information events, festivities and demonstrations (Müller-Bachmann et al., 2022). However, such groups often face stigmatization and criminalization, undermining of group identity, and institutionalized social subordination (Fraser, 2000; Müller-Bachmann et al., 2022). The groups often feel that the media and public willfully misrepresent their beliefs and actions, and (violent) suppression of activism by authorities often relates to an increased feeling of justification of the protest, oftentimes resulting in even more activism (Müller-Bachmann et al., 2022).

The effectiveness of counter movements

In terms of mass formation, possible counter movements have received far less scientific attention (Maguire, 2020; Mayer & Bert, 2017). Many people may realize that the direction society is moving in does not match with core values, such as humanness (e.g., consideration, empathy), critical thinking and freedom (cf. Bennoune, 2020; Stott & Radburn, 2020). Indeed, during the COVID-19 crisis, there has been a global wave of social justice movements that draw attention to the negative effects of a multi-dimensional crisis (Pleyers, 2020). While most of these movements have a strictly non-violent character, the tactics used by these movements range from civil disobedience and (strict) nonviolence, to anti-authoritarian strategies and self-defense and even guerrilla warfare (Sovacool & Dunlap, 2022). Whether or not these movements are effective and what methods are most effective remains a matter of debate (Gulliver et al., 2021). While the authors of this article do not approve of any violence, some writers even argue that violence against a state that has a violence monopoly is sometimes justified and necessary (Gelderloos, 2007). However, recent historical research shows that non-violent approaches are much more effective than violent ones (Janecka, 2021). Regardless, the righteousness of such movements can be debated (Alperstein, 2021). Several authors have claimed that these movements in current times are misinformed and hence see the rise of these movements as dangerous (Sternisko et al., 2020). However, simply claiming that those movements are misinformed and labelling all information not in line with official guidelines as "conspiracy theories" (e.g., Darius & Urquhart, 2021) may be too naïve. Counter movements, often organized in online groups, maybe strongly motivated to be well-informed. In looking at the effectiveness of such movements, it is important to take the psychological aspects into account (Gulliver et al., 2021). In part, effectiveness may depend on the extent to which such groups are able to create space for new social relations, spread awareness, show resilience, have elite support/permission such as that they are shielded from police and military suppression, and are actually able to improve people's lives (Loadenthal, 2017; Sovacool & Dunlap, 2022). Although for obvious reasons a causal relationship between pressure on authorities and change in policies is difficult to determine, there is some evidence to warrant the consideration of a potential relationship (Carty & Onyett, 2006).

Historical research from 1900 to 2006 comparing the effectiveness of in total 323 violent versus non-violent resistance campaigns showed that nonviolent civil resistance was more effective in producing change (Stephan & Chenoweth, 2008). During this time span, violent campaigns were successful in 26% of the cases, whereas non-violent campaigns were successful in 50%.

In the last 10 years of the research, this effectiveness was reduced to only 6% for violent campaigns versus 34 % for non-violent ones (Chenoweth et al., 2011; Kraemer, 2021; Pagnucco, 2022). Countries in which there were non-violent campaigns were 10 times more likely to transition to democracies within five years after those campaigns, than countries with violent campaigns. Interestingly, this was independent of whether the campaign succeeded or failed (Chenoweth et al., 2011). Effectiveness was bigger under conditions of large, diverse and sustained participation, when the movement was able to elicit loyalty shifts among power elites (e.g., army, police, media, business elites), when campaigns entailing more than protests, with variation in methods used, and when campaigns did not descend into chaos or opt for violent methods despite repression(Chenoweth et al., 2011). Preparation of successful campaigns seems crucial, for instance in South-Africa the anti-apartheid movement organized a boycott of white business after preparing for months to become self-sufficient first (Hallward et al., 2017).

The recent decline in effectiveness of non-violent movements might be due to several factors, among others the smaller size of such campaigns, reliance on more symbolic displays of resistance and mass non-cooperation (such as street demonstrations rather than strikes) that do not actually weaken the opponents sources of power, and less disciplined nonviolent actions (Chenoweth, 2021). Sometimes even one person can make a difference (Said, 2005; Shahinpoor & Matt, 2007). Della Porta (2020c) argues that many protests gain momentum and that three kinds of ruptures can be brought about by counter movements, often in succession of each other: cracking, or sudden ruptures; vibrating, contingently reproducing those ruptures; and sedimenting, stabilization of consequences of the rupture. If these historical lessons apply, perhaps effective counter movements could be helpful in turning around the decisions of implementing non-effective and harmful NPIs, thereby buffering the negative effects in the long-term.

5 Adverse Outcomes for Humankind

5.1 Hardship and collective trauma

Next to financial insecurity and hardship for many, as well as increasing inequalities as discussed below, aggressive measures also adversely impact physical and mental health (Ando & Furuichi, 2022; Schippers, 2020; Schippers & Rus, 2021). We will focus here on the result of collective trauma or the “psychological reactions to a traumatic event that affects an entire

society" (Hirschberger, 2018, p. 1). This kind of trauma can affect the collective memory of an entire group and often invokes some kind of sense making (Erikson, 1976; Maitlis & Sonenshein, 2010). The current crisis is no different in that respect, although the scale of collective trauma might be much bigger than seen before (Stanley et al., 2021). Recent research showed that four mental models seem to be associated with the current collective trauma, namely uncertainty, danger, grotesque and misery, as well as four primary emotions, namely grief, disgust, anger, and fear (Stanley et al., 2021). Although people have a propensity to hide negative emotions and trauma, expression of emotions can yield both individual and collective benefits; sharing may alleviate emotional distress and aid in garnering social support (Basinger et al., 2016).

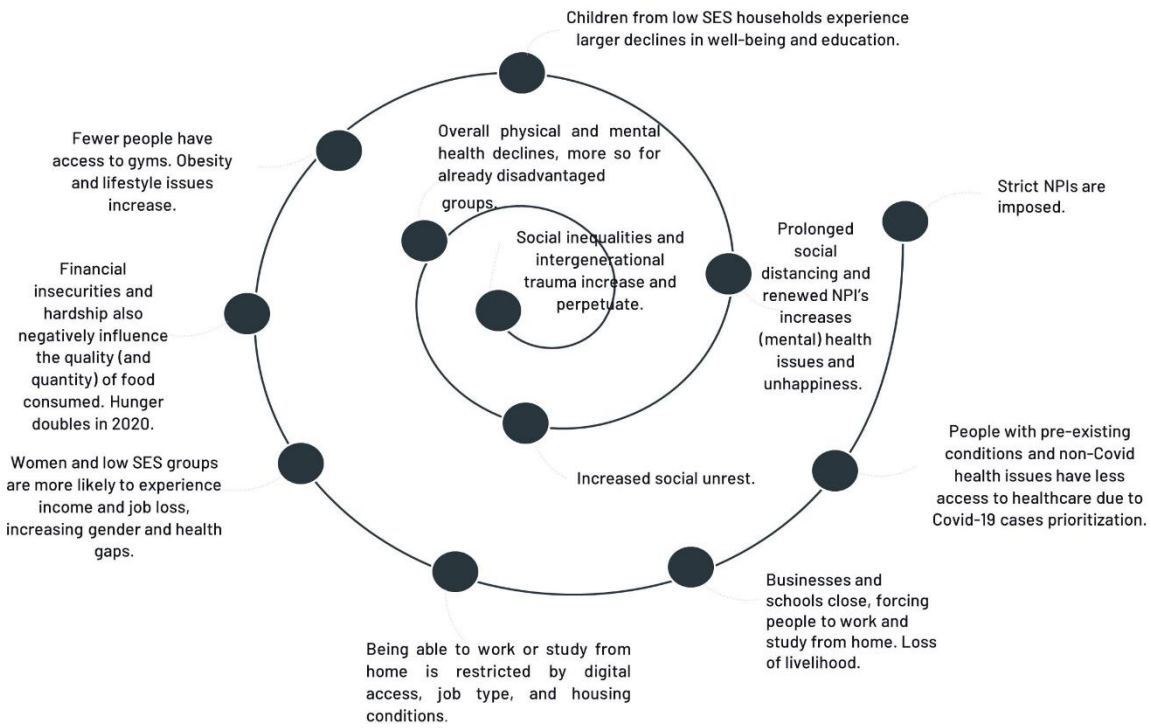
5.2 Conservation of resources theory and broaden and build theory

Conservation of Resources theory (COR) can serve as an integrative theoretical lens for understanding how people gain and conserve resources (Hobfoll, 1989, 2011; Hobfoll et al., 2018). People differ in the extent to which they are good at gaining tangible resources (e.g. money and property) and intangible resources (e.g. strategic relationships to gain power) (Fuller & Marler, 2009). According to COR, both individuals and groups, and even societies as a whole strive to obtain and maintain resources valuable to them (Hobfoll et al., 2018). Formulated in the context of stress and stressful events, COR is a motivational theory, with the premise being that an important human bias is to overweight resource loss and underweight resources gain. This bias stems from an evolutionary need to acquire and conserve resources for survival (Hobfoll et al., 2018). COR has been used to explain stress outcomes in various contexts, including organizational settings, following traumatic stress and for everyday stressors (Hobfoll, 1989, 2001).

Hobfoll speaks of "resource caravan passage ways", meaning that the ecological conditions often determine the extent to which people can create and sustain resources (Hobfoll et al., 2018). Indeed, it has been noted that in general, women were already on a resources loss before the crisis, but that the crisis has exacerbated it, and a resource loss spiral can jeopardize progress towards gender equality (Peck, 2021). For instance, as women work predominantly in service sectors, shutdown of many such sectors has disproportionately affected them, leading to the largest gender-unemployment gap ever recorded (Federal Reserve Bank of St. Louis, 2020), see also (Peck, 2021). This, combined with the increased number of stressors at home, to do

more household chores and care tasks, leads to increased stress, less leisure time and increased chance of burn-out (Peck, 2021). People became more socially conservative during the crisis, in terms of traditional gender role conformity and gender stereotypes, while political ideology remained constant (Rosenfeld & Tomiyama, 2021). Stress occurs when resources are lost. In Western contexts 74 common and important resources are described, including sense of pride, goal accomplishment, hope, personal health, food, help with household chores and childcare, and stable employment (Hobfoll, 1989, 2001). While during crisis access too many of these resources were blocked, people experienced many other stressors and concurrent loss of so many resources has been unprecedented (cf. de Jong et al., 2020), see Figure 2 for a downward spiral in resources).

Figure 2: Downward spiral of rising inequalities resulting from aggressive and prolonged NPI's



This can be traumatic for many people, especially given the unpredictability about the duration and intensity of the situation (Shelef et al., 2022). Fear has been identified as a strong predictor of posttraumatic stress disorder and this is often accompanied by negative thoughts about the self, others and the world (Shelef et al., 2022). This is compounded by a worldwide sense of insecurity, and loss of personal and social security (Kalinowski et al., 2022), leading to

psychological symptoms of grief (Shelef et al., 2022). Also, job loss has been associated with symptoms of grief and loss of meaning in life (Crayne, 2020). Staying-at-home orders are associated with loss of freedom and autonomy as well as loneliness (Bareket-Bojmel et al., 2021), especially when the measures were perceived as coercive (Ranieri et al., 2021). This may also lead to a fear of coercive policies being enforced over a longer or perhaps indefinite amount of time (Kavanagh & Singh, 2020). Fear- and anxiety-related disorders have spiked since 2020 (Santomauro et al., 2021). Overall, both tangible and intangible resources were lost during the crisis, having an impact on physical and mental health (cf. Rosenfeld et al., 2022; Shelef et al., 2022). People that were subject to extreme resource loss (e.g., losing their income, going through divorce, losing access to proper health care and ways to cope) may fall prey to the *desperation principle*. This understudied tenet of COR predicts that when people's resources are outstretched or exhausted, they may enter a defensive self-preservation mode in which they behave increasingly aggressive and seemingly irrational (Hobfoll et al., 2018; Vashdi et al., 2022). They may defensively try to conserve the remaining resources (Hobfoll, 1989). It has been shown that if people are subject to an increased number of stressful events, prevalence of depression symptoms also increased (Suzuki et al., 2018), and major depression is a leading cause of suicide (Hawton & van Heeringen, 2009). Current research indicates that suicide rates may indeed have increased (Ando & Furuichi, 2022), sometimes after an initial decline in suicides (Tanaka & Okamoto, 2021). People with more resources before the pandemic may be better suited for resource gain (Shelef et al., 2022), which can contribute to psychological well-being, health and functioning (Hobfoll et al., 2012). Groups that had fewer resources from the start included minority groups, youngsters, females and individuals with a mental health history, and economic insecurity (Gauthier et al., 2020; Thomas et al., 2020). In the context of massive and worldwide resource-loss, it may be imperative to focus on resource gain, since resource gains become more potent in the face of significant and/or sustained resource loss (Chen et al., 2015). People in comparable circumstances may differ in how resilient they are in dealing with those circumstances (Chen et al., 2015), and some may experience post-traumatic growth (Calhoun & Tedeschi, 1999). Research by Yi-Feng Chen et al. (2021) stresses the role of proactive personality and organizational support in coping with disruptions during COVID-19.

A theory that can explain how people can thrive even in impoverished circumstances is *broaden and build theory* (Fredrickson, 1998, 2001; Fredrickson & Branigan, 2005; Huppert

et al., 2004). This motivational theory asserts that positive emotions and social bonds direct our attention towards longer term benefits (Cohn & Fredrickson, 2006). Its basic tenet is that positive emotions enlarge our attentional scope beyond the present moment, and this in turn aids in seeking out opportunities that go beyond mere survival (Fredrickson, 1998). It can explain why and how some people can go from a downward spiral to an upward spiral by tapping into positive emotional resources, for instance gratefulness (Jiang, 2020). In a study performed during the pandemic among front-line medical staff, it was shown that social support and hope mediate the relationship between gratitude and depression (Feng & Yin, 2021). Taken together, both COR theory and broaden and build theory give theoretical and practical guidance in terms of increasing tangible and intangible resources after (massive) resource loss.

5.1 Prior life circumstances

The extent of harms caused by aggressive and ineffective NPIs may by also be exacerbated by the pre-exiting or induced lack of stability of the social order in a country or region and pre-existing mental health issues (Schippers, 2020)(Alonzi et al., 2020). During the crisis those with pre-existing mental and physical health conditions reported the highest level of emotional distress in terms of anxiety and depression, although mental health deterioration was population-wide (Alonzi et al., 2020). Also, poverty increase in already vulnerable regions made things worse. Additional, extreme events, such as riots and wars may add an extra layer of harm, sometimes on a multiplicative scale (Van Lancker & Parolin, 2020). This can be related to a downward spiral, of loss of livelihood, increased inequalities and mental and physical health decline (See Figure 2).

6 Rising Inequalities

Social inequalities occur when resources within society are distributed unequally, e.g., income, goods, access to information, etc.(Cushing et al., 2015). In the last decades, economic inequality increased in most countries, stabilizing in the 1990s (Neckerman & Torche, 2007), but increasing dramatically since 2020, prompting some authors to refer to this as the “second pandemic” (Fiske et al., 2022). While the focus on making profits has created wealth for large groups of people, resources have become unevenly divided among the total population. There is evidence that the economic inequality increased (Binns & Low, 2021). Although this trend

was already visible before the crisis started (for a review see Neckerman & Torche, 2007), this seems to have accelerated after the start of the crisis (*Global Economic Prospects, June 2020*). While in the last 25 years, 1.1 billion people were lifted from poverty by means of economic growth (Lustig et al., 2002), during the crisis global extreme poverty rose sharply and in October 2021 it was estimated that 100 million additional people were living in poverty (World Bank, 2022). Very early on in the pandemic, warnings were expressed that the negative effects may outweigh possible positive ones (Ioannidis, 2020; Joffe, 2021; Melnick & Ioannidis, 2020; Schippers, 2020) and ways to optimize decision-making (Schippers & Rus, 2021) and alternative ways forward were offered (A. R. Joffe & D. Redman, 2021). Note that other authors disagree and argue that the NPIs are proportional and have substantial benefits (e.g., Koh et al., 2020; Meyerowitz-Katz et al., 2021). It is likely that debate and disagreement will continue, given that assessments on the relative benefits of lockdown are based largely on weak observational data under very complex circumstances.

Inequalities have several consequences for health, well-being and happiness, and longevity (Arora, 2016; Cushing et al., 2015). Countries that let inequality increase have lower happiness rates than countries with higher equality (Frijters et al., 2020; Bartram, 2022). Population well-being, consisting of physical, emotional, and social health, explains variation in life-expectancy. Communities with high well-being are characterized by engaging in healthy behaviors, strong social connections and support systems (Arora, 2016), and happy people live longer (Diener & Chan, 2011), even though the causal mechanisms can be debated. Several meta-analyses have shown a favorable association between psychological well-being and survival (Chida & Steptoe, 2008), and well-being partially mediates the associations of race, poverty, and education with life expectancy (Arora, 2016). Importantly, life satisfaction and optimism about the future, and access to housing, healthcare and perceptions of safety, were also significantly associated with life expectancy (Arora, 2016). Poor housing conditions were related to greater stress and reduced well-being during the COVID-19 crisis (Bower et al., 2021) As psychological well-being is affected both directly and indirectly via the pandemic and the NPIs (i.e. losing one's job and housing, getting a divorce because of the aforementioned, or because of being quarantined for months), this may lead to more inequalities in terms of income, but also well-being (cf. de Jong et al., 2020). The general health and well-being during the crisis has been lowered (for a review see Xiong et al., 2020), especially so for vulnerable groups and disadvantaged countries (McNeely et al., 2020; Yamey

et al., 2021). Below we first discuss the various inequalities affected by the pandemic and the adopted NPIs. We should caution that it is often difficult to disentangle how much of these effects were due to the pandemic versus due to the measures taken. Occasionally the interaction of the pandemic with the measures taken may have had multiplicative negative effects. Then, we discuss options that may help in breaking this trend. In Table 1, we give a non-exhaustive overview of literature and findings regarding inequalities during the COVID-19 crisis.

6.1 Vulnerable populations

Many authorities responding to the pandemic often stated they aimed to protect the vulnerable. However, several adopted measures seem to have especially hurt this group instead of helped. Several measures disrupted and contracted the social networks of older adults during the crisis. Pre-pandemic racial/ethnic network disparities were exacerbated, with negative consequences for physical and mental health outcomes of these groups (Gauthier et al., 2020). As networks are important not only in daily life, but especially in times of crisis, social distancing led to a limited ability to weather the crisis, especially for vulnerable populations (Gauthier et al., 2020). Many countries have chosen to put vulnerable elderly people in complete isolation. This forced social and physical isolation is a serious stressor (Brooks et al., 2020). Resilience may have been further compromised (Holt-Lunstad & Smith, 2012; Holt-Lunstad et al., 2010), creating paradoxical effects (Schippers, 2020). Both regular and routine health care for non-COVID-19 disease was disrupted, posing a threat to health outcomes for many diseases (e.g., Bisht et al., 2020; Barnard et al., 2021). The long-term consequences of the relative neglect of the public health care system, and that people were hesitant to visit their physician for non-COVID-19 problems (Czeisler et al., 2020; Imlach et al., 2021; Lange et al., 2020; Nourazari et al., 2021; Saeki et al., 2022), still remain unfathomed. E.g., it was estimated originally that about 28,5 million operations world-wide were postponed during the initial 12-week peak of the crisis (Collaborative, 2020). Once more, vulnerable populations were hit hardest, increasing pre-existing inequalities (Arnault et al., 2021).

6.2 Economic inequality: The rich got richer, and the poor poorer

Economic inequality has hugely increased exacerbating pre-existing inequalities and this seems a self-reinforcing process as lockdown measures continue or keep being imposed (Binns & Low, 2021; Ferreira, 2021; Krauss et al., 2022; Wikipedia, 2022; Yonzan et al., 2021). Hundreds of millions of people were driven into poverty, while others, individuals and

corporations, gained (Berkhout et al., 2021) This has led to the paradoxical situation that in some countries people were more worried of starvation than of becoming ill from COVID-19 (Krauss et al., 2022). Almost 4 billion people, half of the world population, lives on less than 6.70 dollar a day. A review across four continents showed that restrictive NPIs are especially hard on the poor as they unevenly impact the livelihood and socio-economic activities of those groups (Buheji et al., 2020). A World Bank report concluded: "Taken together, COVID-19 has directly offset the reduction in the [poverty] gap between countries observed from 2013 to 2017." (Yonzan et al., 2021). Income loss was steepest for the poorest 20% of the world, resulting in the largest impact of the COVID-19 crisis for the world's poorest, increasing the global poverty rate from 7.8 to 9.1 percent by the end of 2021 (Sanchez-Paramo, 2021). The effects on inequality and social mobility are expected to be long-term: people who lost income due to the pandemic have been about twice as likely to spend down on assets or savings. Hence, they will be less able to cope with continued or reoccurring income loss. Also, 57% of the people who lost income due to the pandemic have been more likely to go a full day without eating, and the aggregate loss of between 0.3 and 0.9 years of schooling also impacted the poorer families and their economic prospects. Government interventions such as unemployment insurance and benefits for furloughed workers in the short term at least, partially mitigate the effect of the loss of livelihood (Aspachs et al., 2021). In Spain, it has been estimated that without those interventions, inequality would have increased by almost 30% in just one month (Aspachs et al., 2021; World Bank, 2022). However, young people and foreign-born workers profit less from those interventions and experience a large loss of purpose in life (de Jong et al., 2020).

Table 1. *Non-exhaustive overview of the effects on inequality resulting from the non-pharmaceutical interventions enforced in response to the SARS-CoV-2 pandemic. Of note, for several of these effects, it may be difficult to disentangle the impact of the pandemic the measures taken and their interaction.*

Socio-economic status (SES) and ethnic groups	
Estimates that the side effects of attempting to fully mitigate the COVID-19 pandemic will negatively impact life expectancy. Over ten years, the negative life expectancy from socio-economic inequalities alone will be around the equivalent of six unmitigated COVID-19 pandemics. This is not considering the negative effects on life expectancy due to increased mental health problems, suicides, and drug abuse.	McCartney et al. (2020)
The effect of the COVID-19 pandemic and lockdowns differed across SES groups, e.g., groups or counties with lower SES had higher infection incidence and mortality.	Bajos et al. (2021); Clouston, Natale & Link (2021); Gauvin et al. (2022); Wachtler et al. (2020).
Racial minorities (Black, Indigenous, and Hispanic) were more at risk of getting infected and had worse COVID-19 health outcomes during the pandemic. Existing inequalities were exacerbated.	Bajos et al. (2021); Bambra et al. (2021); Barnard et al. (2021); Blundell et al. (2020); Cifuentes et al. (2021); Ribeiro et al. (2021); Liao & De Maio (2021); Perry, Aronson, & Pescosolido (2021); Watkinson et al. (2022)
Children with low SES experienced worse health outcomes during the pandemic due to increased exposure to adverse health determinants	Cifuentes et al. (2021); Gonzalez-Rabago et al. 2021); Parker et al. (2021); Politi et al. (2021); Reboucas, Falcao, & Barreto (2021);

(e.g., tobacco, unsuitable food, changes in physical activity, spending more time in front of the screen, less social contact and more noise.	Ribeiro et al. (2021); Jaspal et al. (2021); Nemati et al. (2021); Sepulveda & Brooker (2021)
People living in areas with higher levels of pre-existing inequalities experienced more adverse effects during the pandemic.	Blundell et al. (2020);Gauvin et al. (2022); Bambra et al. (2020); Cerqua & Lette (2022); Clouston et al. (2021); Liao & De Maio (2021); Malmusi et al. (2022); Tan et al. (2021); Sepulveda & Brooker (2021); Wachtler et al. (2020).
Healthy behaviors (e.g., physical activity, healthy eating) were lower, especially for low SES families.	Gao, Davillas & Jones (2022); Gauvin et al. (2022);
Geographical economic effects of the crisis. Uneven economic effects uncorrelated to the epidemiological pattern. Lower educational levels related to higher mortality for working-aged women and people between 65 and 79 years old during the crisis. The rise in social inequality because of the burden of the disease and the measures have fallen disproportionally on already disadvantaged groups challenges solidarity and social justice.	Alicandro et al. (2021); Bambra et al. (2020); Cerqua & Lette (2022); Clouston et al. (2021); Liao & De Maio (2021); Malmusi et al. (2022); Tan etal. (2021); Sepulveda & Brooker (2021); Stok et al. 2021; Wachtler et al. (2020).
The pre-existing inequalities of refugee teenagers compounded due to the response to the pandemic, with worse (mental) health outcomes, due to severe economic and service disruptions, as well as low social connectedness.	Jones et al. (2022)
Ethnic minorities had a lower COVID-19 vaccine uptake, higher mortality rates and larger decreases in life expectancy.	Andrasfay & Goldman (2021); Watkinson et al. (2022)
Food insecurities arise for low SES groups due to the rise in poverty, unemployment and food prices. In addition to the economic barriers, people living in rular areas also experienced insecurities due to decreased psychical access to food.	Gundersen et al. (2020); Laborde et al. (2020); Niles et al. (2020); Udmale et al. (2020)

Food insecurities lead to an increase in unhealthy eating behaviors (e.g. consuming high caloric products)	Gao, Davillas & Jones (2022);
Digital inequalities led to disparate possibilities during the pandemic such as access to COVID-19 vaccinations, the ability to work or study from home and to maintain social connections with friends and family.	Andrew et al. (2020); Haelermans et al. (2022); Katz et al. (2021); Malmusi et al. (2022); Nguyen et al. (2021); Zachreson et al. (2021)
Gender Inequalities	
Women experienced higher rates of mental health issues and psychological deterioration than men.	Borrescio-Higa & Valenzuela (2021); Gao, Davillas & Jones (2022); Gibson et al. (2021); Utzet et al. (2022); Yerkes et al. (2020)
Women experienced a higher increase in suicide rates than men.	Fisher & Ryan (2021); Manun (2021); Nomura et al. (2021);
Women also more often experienced job loss and/or loss of income than men.	Brzezinski (2021); Christl et al. (2022); Dang & Viet Nguyen (2021); Utzet et al. (2022); Yerkes et al. (2020); Perry, Aronson & Pescosolido (2021); Martinez-Bravo & Sanz (2021)
Gender gaps and unequal distribution of household chores increased during the pandemic. Women reported increased household chores and childcare and decreased leisure time. The propensity to work from home did not differ across genders. In Spain, by May 2020, women from middle-income households with kids experienced 3% larger income loss than men.	Borrescio-Higa & Valenzuela (2021); Brzezinski (2021); Pitzalis & Spano (2021); Yerkes et al. (2020); Martinze-Bravo & Sanz (2021)
Reinforcement of existing gender inequality in academic work. Women were underrepresented as (senior) authors of academic papers during the pandemic, deepening pre-existing inequality. While the	Gorska et al. (2021); Pinho-Gomes et al. (2020); Quak et al. (2021)

quantity of women authored publications seemed to have been on par, quality seemed lower.	
Women were more exposed to the COVID-19 virus than men due to representing most frontline workers. In Spain, the cumulative incidence rate was higher for women than men.	Blundell et al. (2020); Guerrina et al. (2021); Politi et al. (2021)
Males experienced higher COVID-19 mortality rates than females.	Blundell et al. (2020); Ribeiro et al. (2021)
The COVID-19 pandemic caused serious setbacks in advancements in solving problems such as child marriages, gender-based violence female genital mutilation. Estimates show that six months of lockdown led to an additional two million more cases of female genital mutilation, 31 million cases of gender-based violence and the 13 million more child marriages over the next 10 years that wouldn't have occurred otherwise.	Bellizzi et al. (2020);
Age group Inequalities	
The risks of mortality from COVID-19 for people aged 60 and above are significantly higher than for younger people. This lead to a life expectancy decrease in 27 out of 29 countries included in the study.	Aburto et al. (2022); Cifuentes et al. (2021); Politi et al. (2021):
Health Inequalities	
Patients with non-COVID 19 conditions had less access to treatment and preventive measures during the crisis Taken together with other trends, such as privatization of healthcare, already marginalized	Bisht (2020); Blundell et al. (2020)

sections of society were hit harder, leading to worsening existing and creating new health inequalities.	
Physical activity health inequality was increased due to differences in access and availability to engage in physical activities during lockdowns.	Shur et al. (2020)
The switch to remote consultations especially impacted older people, unemployed, people with low SESs, migrants, and men, as these groups were less likely to use remote consultation.	Parker et al. (2021)
People with pre-existing health conditions (e.g., obesity or malnutrition) had worse COVID-19 outcomes. Oftentimes these people also experienced social inequalities and nutritional disparities long before the crisis.	De Lorenzo et al. (2022); Jaspal & Breakwell (2022); Stok et al. (2021)
Mental Health Inequalities	
The crisis increased existing mental health conditions and exacerbated preexisting inequalities in that respect. Financial insecurity mediated some of the effect of SES and mental health outcomes. People with a (family) history of mental health disorder also experienced greater difficulties adjusting after lockdown release. SES inequalities in social network, loneliness and mental health increased. A study in Japan showed positive effect on subjective well-being for socially advantaged people versus negative effects for socially disadvantaged people, widening the gap	Claes et al. (2021); Fineberg et al. (2021); Gagne et al. (2021); Gauvin et al. (2022); Gao, Davillas & Jones (2022); Jaspal et al. (2022); Sudo (2022) Stok et al. (2021)

Economic Inequalities	
Income inequality was mainly created by the policy response to the crisis rather than its health consequences. By early June 2020, the pandemic has generated at least 68 million additional poverty years in 150 countries, mainly among already disadvantaged groups. Additionally, the health consequences worsen income inequality.	Esseau-Thomas, Galarraga & Khalifa (2022)
Working from home increased inequalities in the labor market based on SES, digital access, job type, sector and hierarchical position. Male, older, highly educated and highly paid employees benefited from working from home.	Bajos et al. (2021); Bonacini et al. (2020); Blundell et al. (2020); Cerqua & Letta (2022); Delaporte, Escobar, & Pena (2021); Gao, Davillas & Jones (2022); Martinez-Bravo & Sanz (2021); Zachreson et al. (2021)
Aggressive NPIs increased income inequality and poverty, with vulnerable groups impacted more. In Spain, by May 2020, households in the richest quintile lost about 7% of their income, while the poorest quintile lost 27% of their income.	Palomino, Rodriguez, & Sebastian (2020); Perugini & Vladisavljevic (2021); Shen et al. (2021); Perry, Aronson, & Pescosolido (2021); Stok et al. (2021)
The pandemic did not affect between-country inequality, which continued to decrease as in the previous years.	Deaton, A. (2021)
Educational inequalities	
Educational inequalities emerged or increased in terms of parental income, education, internet access, English and technology skills, and/or previous school performance. Search for online learning resources was substantially larger for areas with higher income, better	Andrew et al. (2020); Bacher-Hicks et al. (2021); Devkota (2021); Grewenig et al. (2021); Haelermans et al. (2022); Katz et al. (2021)

internet access and fewer rural schools in the US. In Germany, daily learning time was halved, from 7.4 hours. This decrease was significantly larger for low achievers, who displaced learning time with TV or computer games. In the Netherlands, where access to internet is better than other countries, with a relatively short school closures of 12 weeks, education learning loss sharply increased for students from disadvantaged households.	

6.3 Economic inequality: The rich got richer, and the poor poorer

Economic inequality has hugely increased exacerbating pre-existing inequalities and this seems a self-reinforcing process as lockdown measures continue or keep being imposed (Binns & Low, 2021; Ferreira, 2021; Krauss et al., 2022; Wikipedia, 2022; Yonzan et al., 2021). Hundreds of millions of people were driven into poverty, while others, individuals and corporations, gained (Berkhout et al., 2021) This has led to the paradoxical situation that in some countries people were more worried of starvation than of becoming ill from COVID-19 (Krauss et al., 2022). Almost 4 billion people, half of the world population, lives on less than 6.70 dollar a day. A review across four continents showed that restrictive NPIs are especially hard on the poor as they unevenly impact the livelihood and socio-economic activities of those groups (Buheji et al., 2020). A World Bank report concluded: "Taken together, COVID-19 has directly offset the reduction in the [poverty] gap between countries observed from 2013 to 2017." (Yonzan et al., 2021). Income loss was steepest for the poorest 20% of the world, resulting in the largest impact of the COVID-19 crisis for the world's poorest, increasing the global poverty rate from 7.8 to 9.1 percent by the end of 2021 (Sanchez-Paramo, 2021). The effects on inequality and social mobility are expected to be long-term: people who lost income due to the pandemic have been about twice as likely to spend down on assets or savings. Hence, they will be less able to cope with continued or reoccurring income loss. Also, 57% of the people who lost income due to the pandemic have been more likely to go a full day without eating, and the aggregate loss of between 0.3 and 0.9 years of schooling also impacted the poorer families and their economic prospects. Government interventions such as unemployment insurance and benefits for furloughed workers in the short term at least, partially mitigate the effect of the loss of livelihood (Aspachs et al., 2021). In Spain, it has been estimated that without those interventions, inequality would have increased by almost 30% in just one month (Aspachs et al., 2021; World Bank, 2022). However, young people and foreign-born workers profit less from those interventions and experience a large loss of purpose in life (de Jong et al., 2020).

6.3 Educational Inequalities

Early in the pandemic, school closures were widespread. In March 2020 schools closed in 138 countries, affecting 80% of students worldwide (Van Lancker & Parolin, 2020). This despite a heated scientific debate regarding the effectiveness of school closures on virus transmission.

Without a clear answer on the effectiveness of school closures, students' education suffered and the "hurt can last a lifetime" (Dorn et al., 2020; for a review see Schippers, 2020; Van Lancker & Parolin, 2020). As early as April 2020 it was stated that school closures would affect poorer children most, as closures also exacerbated food insecurity and the non-school factors (e.g., parental availability for help and supervision, internet access and technology availability, quiet spaces, etc.) that are the primary source of inequalities in educational outcomes (Van Lancker & Parolin, 2020). Even though many schools switched to online education, this did not help much as a substitute. A study in the Netherlands among 350,000 students showed that students made little or no progress during the school closure and learning loss was "mostpronounced among students from disadvantaged homes" (Engzell et al., 2021, p. 1). This was despite that the Netherlands was seen as a best-case scenario, with a relatively short lockdown, equitable school funding and one of the best rates in terms of broad-band access. While for children from high-income families learning might be possible at least theoretically, children from lower income families are faced with numerous hurdles. Besides this, as many parents lost their jobs, these children may be exposed to this stress as well. As "previous recessions have exacerbated levels of child poverty with long-lasting consequences for children's health, wellbeing, and learning outcomes." (Van Lancker & Parolin, 2020, p. 243), the long-lasting consequences should not be underestimated (Cantillon et al., 2017). Recent studies showed a sharp increase in inequalities regarding education (Engzell et al., 2021; Haelermans et al., 2022) and student well-being (Prowse et al., 2021). In addition, home schooling caused high levels of parental stress (Malhi et al., 2021). Taken together, educational inequalities increased sharply, and student as well as parent well-being was at stake during and after the school closures.

6.4 Gender Inequalities

While the year 2020 was earmarked for reflection on gender inequalities, it has been the year that saw an increase in both existing and new gender inequalities (Fisher & Ryan, 2021). The rising gender inequalities are in the domains of health and well-being, home, domestic violence, work and poverty, and leadership (Fisher & Ryan, 2021). Women reported greater stress and anxiety during lockdowns (Debowska et al., 2020), especially women with children (Benassi et al., 2020), and including female students (Prowse et al., 2021). Health and well-being of women were also disproportionally affected, lowering life expectancy, and increasing suicide rates (Fushimi, 2021). Moreover, reports of abuse, self-harm and thoughts of

suicide/self-harm were higher among women (Iob et al., 2020). Women were more likely to experience (physical) aggressive interactions in their dream content (Kilius et al., 2021). Also, women's physical and reproductive health was jeopardized, as many countries reallocated medical care towards COVID-19 patients (United Nations, 2020). Gender-based violence increased at an alarming rate (for a review see Mittal & Singh, 2020). Anxiety and depression tripled for pregnant and postpartum women (Davenport et al., 2020). Mothers were more likely to take on more household chores during the crisis and they were responsible for home schooling (Malisch et al., 2020), and worked on average 5% less, while men worked on average the same number of hours (Collins et al., 2021). Women with young children reduced their work hours four to five time more than fathers (Collins et al., 2021).

In academia, pre-existing inequalities persisted, and new ones arose. While academic gender inequalities were already discussed for quite some time (e.g., Monroe et al., 2008), the crisis increased pre-existing gender inequalities (Woitowich et al., 2021). For instance, in terms of academic output, while men working mainly from home became more productive in the first 10 weeks of the lockdown, and overall research productivity in the US increased by 35%, female productivity dropped by 13%. This productivity gap was found in six more countries (Cui et al., 2022). While women already faced inequity in terms of having a higher teaching load and more service tasks, which are rewarded less than academic publishing, this was exacerbated when teaching and mentoring had to be done online (Cui et al., 2022). This is compounded by women having to take on most household tasks, home schooling, childcare as well as sometimes care for aging parents and extended family (Malisch et al., 2020; Zimmer, 2020). Also, it was predicted that women's poverty rate would rise by 10% globally as a result of the NPIs, as many service jobs were affected (Azcona et al., 2020). Taken together, women experienced more mental health problems, domestic violence, and a larger burden of household and professional tasks.

6.5 Results of inequalities: Increase in stress

The result of rising inequalities may be an increase in stress and resulting mental health problems (Loeb et al., 2021). A meta-analysis indeed showed that income inequality was negatively related to mental health (Ribeiro et al., 2017). In general, humans cause stress on people lower in the hierarchy, and in the last few decades, a lot of research investigated the causes and consequences of this (for a review see Marmot & Shipley, 1996; R. M. Sapolsky, 2004). For instance, Sapolsky researched the question as to why primates (including humans)

cause each other so much stress. Apes and other primates have more stress-related diseases than any other species, and this seems to be because having spare time in these species is used to cause stress to others, usually lower in the hierarchy (Sapolsky, 2005). Stress levels for low-status baboons was significantly reduced when baboons high in the hierarchy were inadvertently killed due to eating tainted meat (Sapolsky & RI, 2004). The extent to which these studies have validity for human society is debatable. For obvious ethical reasons, it is very difficult to do a study in which extreme hierarchical differences are created and subsequently lifted to study the effects. However, the Whitehall studies, stretching over decades show that status differences and inequalities are related to ill health and mortality, even when controlling for lifestyle (Smith et al., 1990), and these differences in health outcomes and mortality even stretched until after retirement (Marmot & Shipley, 1996). Interestingly, this was the case even though mental health for low status workers, working on stressful jobs with little autonomy, increased after retirement (Fleischmann et al., 2019). It goes without questioning that it is imperative to minimize inequalities.

6.6 Reducing inequalities

Good governance, or the actions governments and organizations take to govern society through laws, norms, power or language is key to reduce inequalities in society (Coccia, 2021). Reducing gender inequalities in academia is also important and several policies are promising (Coleman et al., 2022). An Oxfam report suggested to respond to the crisis with several measures increasing equality (Seery, 2021). In general, community development seems to be a promising avenue in this respect (Erickson, 2011). By coordination and integration of the health sector and community development, this may help streamline efforts to influence health and well-being of especially vulnerable groups (Erickson, 2011). Evidence-based policy making may help reducing inequalities (Eden & Wagstaff, 2021) and buffering the negative effects of the crisis. Going forward, citizens and governments should act to create a more equal and sustainable world (Berkhout et al., 2021). Below, we describe what governments could have done better and what can be learned from this crisis. This examination should not be construed as an effort to blame anyone – a blame culture would be a perpetuation of the crisis and the toxic environment that we described above that fosters inequalities. Conversely, it is important to learn from our mistakes so as to correct them and not repeat them, close the circle of the pandemic and be prepared for future pandemics without disrupting life (Ioannidis, 2022).

7 Could we have done better?

We could have done better in our response to the SARS-CoV-2 pandemic. The leadership for management of the pandemic was given to experts who had (or claimed) expertise on COVID-19. This resulted in an exclusive focus on illness and deaths from COVID-19, with implemented and mandated NPIs of unprecedented severity, and which had been recommended against in previous pandemic plans (Aledort et al., 2007; Inglesby et al., 2006; WHO, 2019; WHO, 2006). These NPIs were also implemented without adequate consideration of their collateral effects (as discussed above, and as predicted in previous pandemic plans) and other options open. In short, the response bypassed the lessons learned from past pandemics and other emergencies.

Emergency management (EM) is the prevention and mitigation of, preparedness for, response to, and recovery from emergencies, regardless of the risk/hazard (Redman, 2021). An EM Agency (EMA) is a coordinating agency that coordinates requests from the Subject Matter Agency (the agency dealing with the direct effects of the hazard, here, public health for the SARS-CoV-2 hazard), while also dealing with the indirect effects of the hazard (here, SARS-CoV-2 pandemic and response) (Redman 2021b). The EMA is trained to manage governance, operations, planning, intelligence, logistics, communications, finances, administration, public/private sector collaboration, and education/training activities necessary to manage an emergency (Redman, 2021). Thus, the EMA coordinates the four *simultaneous* EM critical functions: mitigation (separation of the threat from the potential targets or visa-versa), preparedness (building the capability to rapidly respond), response (execution of the capability to prevent injury and loss of life, protect property and critical resources, and meet basic human needs), and recovery (re-establishment of the economy and a state of normal life). Having an EMA coordinate these functions is important because the pandemic is not simply a public health emergency due to the direct effects of severe COVID-19 illness on people, it is a public emergency with direct and indirect effects of the virus and any response to the virus on all of society.

The Emergency Management Process is the same for any public emergency, including a pandemic. By following the process, the EMA, unlike the public health medical experts, is specifically trained to optimize the response. The seven EM process steps that must occur in any public emergency, and how these should have been taken for the SARS-CoV-2 pandemic, are shown in Table 2 (Joffe and Redman 2022; Redman 2021b). By not following the

established EM process, the wrong aim, governance, mission analysis, and courses open were more likely to be selected, and there was no published pandemic plan (Redman 2021b). Most, if not all, of the collateral damage and exacerbation of inequality discussed above was predictable and should have been considered in cost-benefit analyses for all possible courses open (Joffe 2021; Joffe and Redman 2022; WHO 2019; WHO 2006; Aledort et al. 2007; Inglesby et al. 2006).

Of interest, others have come to the conclusion that crucial parts of the EM process were missed during the pandemic response, although these authors did not recognize that these were components of the EM process, and that they were, so to speak, re-inventing the wheel (Joffe, 2021; Schippers & Rus, 2021; Zweig et al., 2021). For example, discussions of cognitive biases (e.g., escalation of commitment, identifiable lives, present, availability, and anchoring biases), information-processing failures (e.g., groupthink, the culture of fear), better frameworks, focused protection, weighing of competing priorities, and reflexivity ("a deliberate process of discussing team goals, processes, or outcomes") all address issues the EM process is designed to deal with (Godfrey-Smith, 2021; Joffe, 2021; Jung et al., 2021; Mulgan, 2022; Schippers & Rus, 2021; Kulldorff & Bhattacharya 2021). In Table 3 we mention some priorities we believe the EM process would have discovered to enable a response with far less collateral damage, and some priorities at this point of endemic SARS-CoV-2 necessary for recovery.

Table 2. ***The Emergency Management process: Seven steps and how they should have been applied during the SARS-CoV-2 pandemic.***

Steps in the EM process	Specifics of this step during the SARS-CoV-2 pandemic
1. Identification of the hazard.	The hazard is SARS-CoV-2.
2. Selection and maintenance of the aim.	The aim is to minimize the impact of SARS-CoV-2 and our response on the society of the jurisdiction. The aim was not necessarily "to flatten the curve" or "to protect the medical system", which may be included in objectives.
3. Establish a Governance Task Force, to provide leadership for all policy, programs, and actions taken, with many diverse stakeholders involved, and led by the most senior government official (e.g., the provincial premier in the provinces of Canada).	Governance Task Force was not assembled, and public health officers and medical advisors had undue influence.
4. Risk/Hazard assessment.	The risk from SARS-CoV-2 was very early on known to be extremely age-dependent (especially in older adults with comorbidities), and the potential impacts on critical infrastructure (including healthcare) predictable.
5. Mission analysis to determine the *objectives* of *what* needs to be done.	For SARS-CoV-2 this includes tasks given (pre-written pandemic response plans) and tasks implied required to meet the aim. This included maintaining confidence in government (by diminishing fear, ensuring mutual aid, and ensuring constant communications), protecting seniors, and protecting critical infrastructure and essential services (e.g., new medical surge capacity, full continued education, continuity of business and economy).

6. Defining courses open/options to determine *how* the mission analysis objectives can be met.	This entails determining courses open for each grouping of tasks, as determined by assigned teams with appropriate diverse expertise (to prevent groupthink). Each course open has a full assessment of cost-benefit to justify options, and plan for solutions to expected collateral damage.
7. Public issuing of a written comprehensive evidence-based Response Plan.	Issuing a written Pandemic Response Plan forms the basis of confidence in government by transparently demonstrably justified due diligence.

References: Joffe and Redman 2022; Redman 2021b; Redman 2022

Table 3. ***Examples of emergency management function priorities in addressing the SARS-CoV-2 pandemic.***

EM function	Priorities at the Start of the Pandemic	Priorities mid-2022 for Endemic SARS-CoV-2
Preparation	Define the mission: to ensure minimum impact of SARS-CoV-2 on society as a whole. Establish a Governance Task Force as the single decision-making body for policy, programs, and actions, with broad diverse representation, led by the Premier, and coordinated and supported by the Emergency Management Agency. Release a comprehensive written Pandemic Response Plan.	Define the mission: to ensure minimum impact of endemic SARS-CoV-2 on society as a whole, *and* to recover from the lockdown-based response collateral damage. Establish the appropriate Governance Task Force, and disband other advisory groups. Release a comprehensive written Pandemic Response and Recovery Plan.
Mitigation	Focused protection of the most vulnerable: a plan for long-term care homes and for those in the community aged ≥60 years with multiple comorbidities.	Voluntary focused protection: understand that the risk for those aged <60 years is similar to that from seasonal influenza.

	Plans for socially vulnerable groups: e.g., temporary housing support to reduce household crowding.	
Response	Ensure critical infrastructure is ready for people who get sick, including new surge capacity in hospitals so that continuity of the medical system is ensured. Ensure equitable access to healthcare.	Removal of fear of SARS-CoV-2 and of each other: ensure understanding of risk in relation to other daily risks, by age group and comorbidity. Removal of fear of future use of NPIs: ensure understanding of accumulated evidence about trade-offs and efficacy in order to end talk of future mandated lockdowns, quarantine of exposed people, school closures, community masking, and border closures. Establish capabilities for endemic SARS-CoV-2: new healthcare surge capacity without plans to sacrifice healthcare for all other conditions.
Recovery	Reduce fear with daily information presented with context including plans for surge capacity, give hospitalizations and death numbers with denominators, by age group, in comparison to other risks causing deaths annually, and without a focus on raw case counts. Give evidence on the cost-benefit balance of NPIs and lockdowns: explain the difficult trade-offs involved and the justification for focused protection.	Develop a detailed plan to overcome the impacts from the use of fear and NPIs/lockdowns on mental health, societal health, our children's education and development, missed/delayed diagnosis and treatment of medical conditions, government debt, confidence in the economy, etc. Replace fear with confidence by using the EM process, with cost-benefit analysis of all recovery options open, improved communication, and a written plan that is transparently demonstrably justified by due diligence.

References: Joffe and Redman 2022; Redman 2021b; Redman 2022

8 Discussion

8.1 Possible ways forward

Governments and public health authorities around the world have felt the urgency to impose decisions on people, while having trouble using evidence-based decision and policy making (Eden & Wagstaff, 2021; Focacci et al., 2022; Schippers & Rus, 2021). This has proven to be quite harmful to many groups in society (Abbasi, 2020; Schippers, 2020). Many scientists also went along with the narrative that the most aggressive NPIs were necessary for the greater good, for instance experts giving advice on how to modify behavior (e.g., Bavel et al., 2020b; Focacci et al., 2022). Others have pointed out that the debate has been highly polarized and should ideally be more open-minded and nuanced (Escandón et al., 2021). It seems that society has fallen prey to groupthink (Joffe, 2021), and that the entrainment of these responses caused the perpetuation of dysfunctional entrenched patterns in responding to the pandemic (Schippers & Rus, 2021). Even so, it seems more important than ever to uphold and renew important values that societies fare by, to enhance well-being of their citizens (Gupta et al., 2021). Healing society should focus on people's dignity, rights, values, and humanity (Gupta et al., 2021). At the same time, it becomes imperative to use evidence-based policy and decision making (Eden & Wagstaff, 2021; Rubin et al., 2021), such as reflexivity (Schippers & Rus, 2021), as used in the emergency management process (Redman, 2021).

It is key to restore health and well-being of the wider population, now more so than ever, and create a positive environment in which people can thrive (de Jong et al., 2020). A recent paper even proposed that well-being should be the goal of governments (Frijters et al., 2020). Next to reversing the most aggressive and ineffective policies (Ioannidis, 2022; Joffe, 2022), the way people cope with the situation is important (Schippers, 2020, Freyhofer et al, 2021). Although most people seem to be negatively affected in terms of health and well-being, recent research show that personality differences may play a role in the extent to which people are optimally dealing with the situation (Yi-Feng Chen et al., 2021). For instance, the extent to which people score high on proactive personality seems to enhance their performance and well-being during the COVID-19 crisis situation (Yi-Feng Chen et al., 2021). People that score high on proactive personality are better at spotting opportunities and acting upon them (Bateman & Crant, 1993). They also are better able to foresee consequences and risks inherent in actions that they take and anticipate on them, affecting environmental change (Crant et al., 2016). Importantly, in the last few years for many people access to intangible resources such as social support, and social

belonging were thwarted, as well as access to tangible resources such as income, livelihood, and access to (healthy) food. Loss spirals gain in momentum and magnitude once resource losses accumulate, while resource gain cycles tend to develop slower and are weaker (Hobfoll et al., 2018). This may explain why it seems easier to widen the inequality gaps, but these may take years and years to close. For instance, while it was estimated before the crisis that closing the gender gap could take up to 99.5 years, after the crisis it was estimated to take 135 years (Kalia, 2021; World Economic Forum, 2021).

8.2 Collective healing and restoring meaning

What is needed in the current situation might be collective healing (Saul, 2013; cf. Conti, 2021). While programs such as Eye Movement Desensitization and Reprocessing (EMDR; Shapiro & Brown, 2019), brainspotting (Grand, 2013) and neurosculpting (Wimberger, 2015) may be effective for relieving (complex) trauma (for reviews see D'Antoni et al., 2022; Gurda, 2015), more scalable positive psychology solutions are needed (Frijters et al., 2020). Many people will feel the need to reinstate a sense of meaning in life (de Jong et al., 2020). Scalable solutions may entail for instance life crafting (reflecting on, setting goals and undertake actions for important areas of life) to find meaning in life, as a written guided online intervention (Schippers & Ziegler, 2019), or via a chatbot (e.g., Dekker et al., 2020; Hoermann et al., 2017). Gratitude and grit may restore a sense of meaning in life and has been related to decreased suicidal ideations (Kleiman et al., 2013). The relationship between gratitude and well-being is well-known (Wood et al., 2010), and it seems that the connection between these is via social connectedness and meaning in life (Liao & Weng, 2018). Communities could investigate possibilities to help many people via scalable solutions (de Jong et al., 2020; Schippers, 2020; Schippers & Rus, 2021). For instance, life crafting and other positive psychology and mental health interventions, delivered online or via a chatbot, could be a scalable solution and "first aid" for people experiencing issues such as anxiety, depression and loss of purpose in life (de Jong et al., 2020; Dekker et al., 2020). Goalsetting also seems promising in terms of reducing the gender and ethnic minority achievement gap for specific populations of students (Schippers et al., 2015). Any interventions need to be rigorously tested for effectiveness and they should preferably be done in concert with other positive psychology interventions tackling educational inequalities (for a review see Easterbrook & Hadden, 2021). At the same time, it is advisable to radically increase voluntariness of measures. Giving people a choice instead of forcing policies upon them, might make for much more effective interventions. For instance when

people work from home voluntarily, they experience fewer adverse effects of teleworking (e.g., Kaluza & van Dick, 2022).

In terms of increasing the base from which decisions are made, less centralized decision making may be desirable, as envisioned in the EM process. This could be achieved by increasing diverse citizen engagement in (global) problems (Carpini et al., 2004), and grass roots movements. In light of the many authoritarian tendencies associated with the pandemic response, it may be worth salvaging democracy (Afsahi et al., 2020; Dostal, 2022; Stoker & Evans, 2022; Ioannidis & Schippers, 2022), and increasing democratization of companies post COVID-19 (Newman & Freilekhman, 2020). The question should be who are best suited to fight the crisis and if it may be better to leave it up to the people's own sense of responsibility to take action after carefully laying out the pros and cons of behavior (Elm & Sarel, 2021). Finally, we should acknowledge that for many of the proposed interventions, we would benefit from having stronger evidence from large (cluster) randomized trials, to understand where they may work, and how much effectiveness we can expect in different populations and circumstances. While the pandemic led to many thousands of randomized trials of drugs, biologics, and vaccines (Hirt et al., 2022; Janiaud et al., 2021), only a dearth of trials were performed on NPIs (Cristea et al., 2020) and the research agenda on psychological and social-level interventions was even more thin. This is a deficiency that needs to be remedied.

9 Conclusion

As the COVID-19 crisis and particularly the response with unprecedented severity and duration of NPIs are related to many negative side effects and seem to increase inequalities for billions of people worldwide (Marmot & Allen, 2020), it becomes imperative to address the negative effects in terms of stress, health and trauma for vulnerable populations (Whitehead et al., 2021). The economic fall-out and consequences for inequality may be felt for years to come (Whitehead et al., 2021). Governments should be well-advised to take well-being as a spearhead for decision-making in the upcoming years (Frijters et al., 2020). It is our hope that with effective interventions the tide may be turned.

10 Author contributions

MS played the primary role in the conception of the manuscript, and wrote, reviewed, and revised the manuscript. JI contributed to writing the manuscript, identifying studies on inequalities, and editing the manuscript. AJ wrote the paragraph on "Could we have done better" and crafted Table 2. AJ also contributed to writing and editing the manuscript.

11 Conflict of Interest

The authors declares that the research was conducted in the absence of any commercial or **financial** relationships that could be construed as a potential conflict of interest.

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PRODUKTIE 9

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The performance of the SARS-CoV-2 RT-PCR test as a tool for detecting SARS-CoV-2 infection in the population

Dear Editor,

Worldwide, detection and monitoring of SARS CoV-2 infection continues to be based on results of the real-time reverse-transcription polymerase chain reaction (RT-PCR) test. A recent scoping review in this journal reported that assessment of the diagnostic accuracy of the RT-PCR test for SARS-CoV-2 has been less than perfect [1]. We analysed real-world data from a large laboratory in the city of Münster (population 313,000), Germany, derived from a single fully automated high throughput RT-PCR platform (cobas SARS-CoV-2 RT-PCR system, Roche Diagnostics) utilizing the same two gene targets for the entire study period (weeks 10-49, 2020). This laboratory performed about 80% of all SARS-CoV-2 RT-PCR tests in the Münster region during this time. We explored changes in the percentage of positive RT-PCR tests (positive rate) over time. In addition, we assessed the influence of covariates such as age, sex, calendar time, and symptoms at the time of first RT-PCR test on the distribution of cycle threshold (Ct) values.

Nearly all swab specimens were tested within 24 hours of collection. The tests and their interpretation were carried out in accordance with the Roche cobas SARS-CoV-2 emergency use authorization (EUA) protocol, the specific targets of the test being the open reading frame (ORF) 1ab and the pan-Sarbecovirus E genes. The limit of detection, defined as the concentration of analyte that will be detected in 95% of replicate tests was 0.007 median tissue culture infectious doses (TCID50) per ml for target 1 and 0.004 TCID50/ml for target 2, corresponding to Ct values of approximately 33 and 36, respectively (cobas® SARS-CoV-2 package insert, version 1.0).

RT-PCR tests that had not crossed the positivity threshold after the 40th cycle were reported as "negative". The Ct value is inversely proportional to the initial amount of target nucleic acid and is thus a relative indicator of the concentration of viral particles in the clinical specimen. An increase in Ct value of three points indicates that the initial amount of viral particles was smaller by a factor of about ten.

We categorized our population-based Ct values according to the recommendations of the UK Office for National Statistics (ONS) COVID-19 household survey as < 25 and ≥ 25 [2]. Since there has been some discussion regarding this Ct-threshold [3-5], we performed a second categorization using a cutoff of < 30 versus ≥ 30. For a small subset of 58 people, sufficient clinical information was available to allow classification as symptomatic or asymptomatic.

Of 162,457 tested individuals, 4,164 (2.6%) had a positive RT-PCR test. The positive rate was lower among children aged 0-9 years (2.2%) and among adults aged 70 or more (1.6%), compared to the intermediate group aged 10-69 years (2.8%). The positive rate was strongly linked to the national SARS-CoV-2 test strategy. During the first and third phase of national testing, predominantly symptomatic people were tested. During these phases, the positive rates were higher than during the intermittent second phase corresponding to the summer season, when predominantly asymptomatic individuals were tested. The positive rate during the third phase was considerably higher than during the first phase. During the peak of testing asymptomatic individuals, only 0.4% tested positive with a mean Ct value of 28.8. Higher mean Ct values were observed among children aged 0-9 years (28.6) and adults above 70 years (27.0). Only 40.6% of positive tests showed Ct values below the threshold of 25, indicating a likelihood of the person being infectious (**Table 1**). In the small group of individuals for whom clinical information was available, symptomatic subjects had a markedly lower mean Ct value of 25.5 compared to asymptomatic subjects, who showed a mean Ct value of 29.6 (**Figure 1**).

Most positive tests in our sample showed Ct values of 25 or higher, indicating a low viral load. Ct values were on average lower in symptomatic than in asymptomatic individuals. Our results are similar to the observations made in the ONS Survey with consistently low positive rates (0.06%) during the summer months,

Table 1
Characteristics of people who underwent PCR testing in the region of Münster, North Rhine-Westphalia, Germany, March 26 - December 6, 2020

	Number of tests[1)]	Positive tests		Mean Ct value among positive tests[2)]		Percentage of positive tests with Ct values[2)]	
	N	N	%	Mean	SD	< 25	<30
All	162,457	4164	2.6	26.5	5.2	40.6	69.6
Men	70,043	1981	2.8	26.4	5.3	42.0	69.6
Women	92,113	2165	2.4	26.6	5.1	39.4	69.5
Unknown	301	18	6.0	27.4	5.2	38.9	66.7
Swab site							
Nose & throat	8637	222	2.6	25.9	5.4	43.0	72.9
Throat	7059	151	2.1	26.2	4.5	41.7	77.2
Unspecified/other	146,761	3791	2.6	26.6	5.2	40.4	69.1
Age group							
0-9	9978	222	2.2	28.6	4.7	21.1	56.5
10-19	15,200	536	3.5	26.8	4.9	38.2	71.4
20-29	21,613	745	3.5	26.4	5.1	41.6	69.4
30-39	21,830	572	2.6	26.3	5.1	42.7	72.3
40-49	21,373	600	2.8	26.3	5.4	43.8	69.1
50-59	25,367	665	2.6	26.0	5.3	44.4	72.9
60-69	17,460	351	2.0	26.0	5.1	46.0	73.5
70-79	12,155	214	1.8	27.1	5.2	35.3	65.8
80-89	13,196	185	1.4	26.8	5.2	37.4	64.5
90-99	3699	55	1.5	27.0	5.4	37.0	63.0
100+	29	1					
unknown	557	18	3.2	31.3	4.9	11.8	29.4
Calendar week							
10-19	12,985	305	2.4	28.7	5.1	22.1	46.8
20-44	132,488	2418	1.8	26.5	5.2	40.5	69.6
45-49	16,984	1441	8.5	26.4	5.1	41.8	70.7
Specific phases of the pandemic[3)]							
Peak 1st wave	2190	36	1.6	27.8	5.4	26.5	55.9
Traveler return	16,874	68	0.4	28.8	5.5	26.9	55.2
Peak 2nd wave	4022	367	9.1	26.6	5.1	39.5	69.8

Legend table: SD = standard deviation
1) only persons with tests that were clearly either positive or negative were included
2) among 4164 people tested positive, the Ct value was available for 3810 people (91.5%); Ct values were not retrievable for positive tests during the calendar weeks 12-13 and 16-25 in 2020
3) Peak of 1st wave in weeks 12-13 (16.-29.3.2020); proxy weeks 13-14; unselective testing in weeks 33-34 (peak of tests for traveler return); peak of 2nd wave in weeks 50-51 (7.-20.12.2020), proxy weeks 48-49

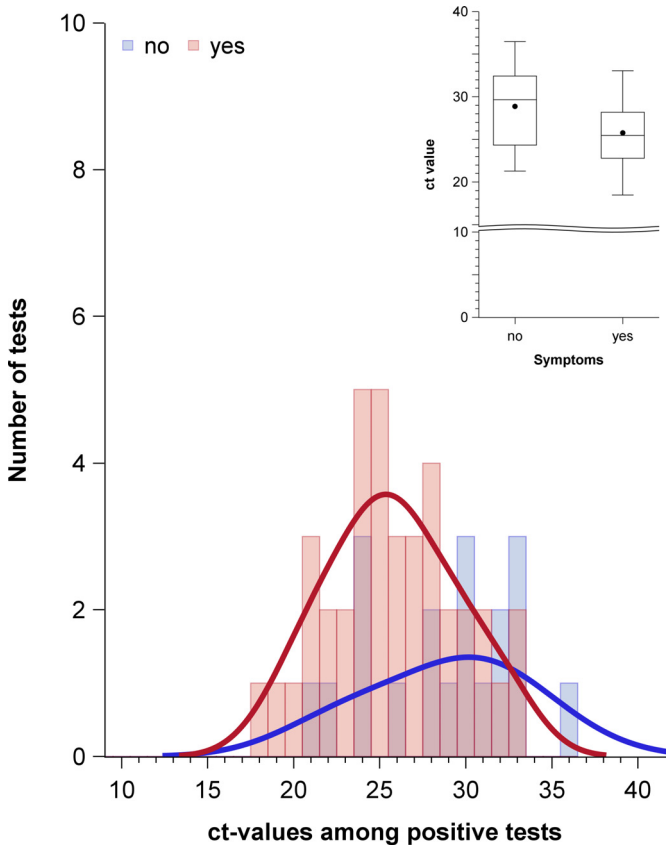

Figure 1. Ct value distribution among symptomatic and asymptomatic individuals´with positive tests in the region of Münster, North Rhine-Westphalia, Germany, 2020
Legend: "no" means "no symptoms", "yes" means "symptoms"; dots in the box plot indicate mean values and horizontal lines in the boxes indicate median values. Asymptomatic individuals : n=19, median 29.6, mean 28.8, SD 4.3; symptomatic individuals: n=39 median 25.5, mean 25.8, SD 3.7

followed by a rise to more than 1% by the end of October 2020. A substantial proportion (45%-68%) of test positive individuals in the UK did not report symptoms at the time of their positive PCR test [6].

In light of our findings that more than half of individuals with positive PCR test results are unlikely to have been infectious, RT-PCR test positivity should not be taken as an accurate measure of infectious SARS-CoV-2 incidence. Our results confirm the findings of others that the routine use of "positive" RT-PCR test results as the gold standard for assessing and controlling infectiousness fails to reflect the fact "that 50-75% of the time an individual is PCR positive, they are likely to be post-infectious" [7].

Asymptomatic individuals with positive RT-PCR test results have higher Ct values and a lower probability of being infectious than symptomatic individuals with positive results. Although Ct values have been shown to be inversely associated with viral load and infectivity, there is no international standardization across laboratories, rendering problematic the interpretation of RT-PCR tests when used as a tool for mass screening.

Declaration of Competing Interest

Paul Cullen has received speaker's fees from Roche Diagnostics. None of the other authors declares any conflict of interest.

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PRODUKTIE 10

WET van ……..…….,
houdende nadere wijziging van de Wet
Uitvoering Burgerlijke Uitzonderingstoestand
(S.B. 2020 no. 151, zoals gewijzigd bij
S.B. 2021 no. 20)

ONTWERP

DE PRESIDENT VAN DE REPUBLIEK SURINAME,

In overweging genomen hebbende, dat het noodzakelijk is de Wet Uitvoering Burgerlijke Uitzonderingstoestand (S.B. 2020 no. 151, zoals gewijzigd bij S.B. 2021 no. 20), nader te wijzigen;

Heeft, de Staatsraad gehoord, na goedkeuring door De Nationale Assemblée, bekrachtigd de onderstaande wet:

ARTIKEL I

In de Wet Uitvoering Burgerlijke Uitzonderingstoestand (S.B. 2020 no. 151, zoals gewijzigd bij S.B. 2012 no. 20) worden de volgende wijzigingen aangebracht:

A. In artikel 1 wordt na onderdeel f een nieuw onderdeel g toegevoegd, luidende als volgt:
   g. besloten plaats: een niet openbare en een niet voor eenieder toegankelijke plaats, niet zijnde een woning.

B. Na artikel 6 wordt een nieuw artikel 6a toegevoegd, luidende als volgt:

Bijzondere maatregelen bestrijding Covid-19 pandemie
Artikel 6a

1. Onverminderd het bepaalde in artikel 6 kan de Regering bij presidentieel besluit in verband met de bestrijding van de Covid-19 pandemie bijzondere maatregelen krachtens dit artikel nemen.

2. Bij presidentieel besluit worden de voor het publiek toegankelijke en besloten plaatsen als bedoeld in artikel 1 onder e en g aangewezen, daaronder begrepen de plaatsen waar arbeid wordt verricht of pleegt te worden verricht of ten aanzien waarvan redelijkerwijze kan worden vermoed dat aldaar arbeid wordt verricht, die slechts onder de in dat presidentieel besluit gestelde voorwaarden voor personen mogen worden opengesteld, toegankelijk zijn of om op die plaatsen aanwezig te zijn.

3. Tot de in lid 2 gestelde voorwaarden behoren in ieder geval dat voor de toegang tot de in dat lid bedoelde plaatsen of voor het aldaar aanwezig zijn, de personen bewijs moeten kunnen leveren van volledig gevaccineerd zijn tegen SARS-COV-2 of van een negatieve SARS-COV-2-RT PCR test of een in dat presidentieel besluit door de overheid erkend SARS-COV-2 antigeen-sneltest, die niet ouder dan 24 uur is. De in de

eerste volzin genoemde verplichting tot overlegging van een bewijs van vaccinatie of van de daarin genoemde testen is niet van toepassing op:

a. een persoon tot en met de leeftijd van twaalf jaar of
b. een persoon waarvan wegens medische gronden vaccinatie tegen SARS-COV-2 of het uitvoeren van genoemde testen ongewenst is of achterwege behoort te blijven, zulks blijkende uit een door een medische specialist afgegeven verklaring of
c. een persoon met religieuze gewetensbezwaren.

4. Ten aanzien van de toegang tot plaatsen waar arbeid wordt verricht of pleegt te worden verricht of ten aanzien waarvan redelijkerwijze kan worden vermoed dat aldaar arbeid wordt verricht, alsmede de toegang tot bepaalde andere dan in lid 2 genoemde plaatsen kan, ten aanzien van de vereiste van volledige vaccinatie en in afwijking daarvan, bij presidentieel besluit worden bepaald dat kan worden volstaan met een eerste vaccinatieprik, in de gevallen waarbij voor een volledige vaccinatie meer dan één keer dient te worden gevaccineerd. De toegang met de eerste vaccinatieprik is toegestaan tot de datum op de vaccinatiekaart waarop de tweede tevens laatste vaccinatieprik dient te zijn ontvangen.

5. De werkgever of de eigenaar of het hoofd of de bestuurder en het opzichthoudend personeel of degene die verantwoordelijk is voor de in lid 2 bedoelde plaatsen of die bevoegd is tot het treffen van voorzieningen met betrekking tot de toegang daartoe, draagt zorg dat de personen aan wie toegang wordt verleend tot die plaatsen of om aldaar aanwezig te zijn, voldoen aan de krachtens de leden 2 en 3 gestelde voorwaarden.

6. Het is degene die niet voldoet aan de bij of krachtens de leden 2 en 3 gestelde voorwaarden verboden, zich de toegang te verschaffen of aldaar aanwezig te zijn tot de daarin bedoelde plaatsen.

C. In artikel 9 lid 1 en artikel 12 lid 1 wordt de zinsnede ‘krachtens artikel 6’ gewijzigd in: krachtens artikel 6 of artikel 6a.

ARTIKEL II

1. Deze wet wordt in het Staatsblad van de Republiek Suriname afgekondigd.

2. Zij treedt in werking met ingang van de dag volgende op die van haar afkondiging.

3. De Ministers van Justitie en Politie, van Arbeid, Werkgelegenheid en Jeugd en van Volksgezondheid zijn belast met de uitvoering van deze wet.

Gegeven te Paramaribo, de ……

CHANDRIKAPERSAD SANTOKHI

WET van ……..…….,
houdende nadere wijziging van de Wet
Uitvoering Burgerlijke Uitzonderingstoestand
(S.B. 2020 no. 151, zoals gewijzigd bij
S.B. 2021 no. 20)

MEMORIE VAN TOELICHTING

(1). Algemeen

In december 2019 stak in de regio Wuhan in China een nieuw coronavirus de kop op, in aanvang als (novel-coronavirus) 2019-nCoV aangeduid en inmiddels formeel SARS-CoV-2 genaamd (severe acute respiratory syndrome coronavirus).
Op 30 januari 2020 had de Wereldgezondheidsorganisatie (WHO) de uitbraak tot «*Public Health Emergency of International Concern*» uitgeroepen. De WHO heeft de uitbraak van het virus op 11 maart 2020 tot pandemie verklaard en de lidstaten opgeroepen om alles te doen wat nodig is in hun nationale context om de verspreiding van het virus tegen te gaan, door in overleg met experts te bepalen welke maatregelen daartoe in de nationale situatie genomen moeten worden.

In maart 2020 is officieel het eerste geval van besmetting met het SARS-COV-2 virus in Suriname gemeld. Sedertdien zijn door de Regering in de verschillende sectoren, in het bijzonder de gezondheidssector, diverse ingrijpende maatregelen getroffen om de verspreiding van het virus en de gevolgen ervan zoveel als mogelijk te minimaliseren.
De grondslag van de maatregelen, is terug te voeren tot de Wet Uitvoering Burgerlijke Uitzonderingstoestand en deze maatregelen behelzen alle sectoren van de samenleving en zijn gericht op de beteugeling van de verspreiding van het virus, waarbij de vrijheid van de burgers in verband met die maatregelen eveneens seldom ongemoeid is gelaten.
Na langer dan een jaar is de volledige beteugeling van dit virus nog ver te zoeken en zijn de gevolgen in bijna alle sectoren van de samenleving, in het bijzonder de gezondheidssector, desastreus, getuige de vele duizenden besmettingen en honderden doden. De financieel-economische gevolgen voor het land zijn bekend; de economie is nimmer zo diep geraakt als door deze pandemie.

Tot een van de middelen in de strijd tegen het SARS-COV-2 virus is de ontwikkeling van vaccins tegen dit virus. Wereldwijd zijn verscheidene vaccins ontwikkeld die tot op zekere hoogte bescherming bieden tegen de gevolgen van het virus.
Variëren van tussen de 60% en 90% kunnen de ontwikkelde vaccins bescherming bieden tegen de ernstige gevolgen van het virus (zie rapporten… ???).
In Suriname is tot op het moment van de voorbereiding van de ontwerpwet een viertal vaccins (Pfyser, Astra-Senecca, Sinopharm en Moderna) voor de samenleving kosteloos beschikbaar. De overheid die grondwettelijk, maar ook op grond van haar internationale verplichtingen ervoor moet zorgdragen dat de lichamelijke en geestelijke gezondheid van de bevolking zo goed mogelijk moet zijn gewaarborgd, in het bijzonder door het treffen van maatregelen ter voorkoming, behandeling

en bestrijding van epidemieën, heeft dan ook ervoor gezorgd dat de vaccins tot een van de mogelijkheden voor de Surinaamse samenleving behoort om het virus te bestrijden.
Over de effectiviteit en betrouwbaarheid van bedoelde vaccins in de strijd tegen het SARS-COV-2 virus kan gemakshalve worden verwezen naar de autorisatie/goedkeuring die deze vaccins hebben gehad van de Wereldgezondheidsorganisatie (WHO) om te worden toegepast. De WHO gaat ervan uit dat van de geautoriseerde/goedgekeurde SARS-COV-2 vaccins, is aangetoond dat zij veilig en effectief zijn bij het voorkomen van ernstige ziekten en overlijden als gevolg van de infecties door het virus. Wereldwijd wordt, ten aanzien van de bestrijding van COVID-19 dan ook het accent gelegd op een zo hoog mogelijke percentage vaccinatiegraad bereiken (minimaal 70%) voor de samenleving en daarmee een betere bescherming van de bevolking als geheel tegen de gevolgen van het virus.
Benadrukt dient te worden dat de bescherming begint bij het individuele lid van de samenleving dat is gevaccineerd, dat daardoor niet ziek of minder ernstig ziek kan geraken, de kans op ziekenhuisopname en overlijden, alsmede de kans op besmetting van een ander behoorlijk reduceert. Tegelijkertijd is het taak en de verantwoordelijkheid van de overheid om ervoor te zorgen dat de samenleving gezond blijft en dus een goede gezondheidszorg steeds gewaarborgd moet zijn.
Op grond van de huidige mogelijkheden en vooruitzichten met betrekking tot de aanpak van het SARS-COV-2 virus, is vaccinatie tegen het virus van het overgrote deel van de bevolking het enige redmiddel om uit deze pandemie te geraken. Het voorgaande kan alleen worden gerealiseerd, indien er een grote mate van bereidwilligheid bestaat om zich te laten vaccineren, hetgeen thans niet het geval is ondanks de uitputting van alle mogelijke middelen en manieren daartoe.
De gevolgen zijn nog steeds merkbaar en nemen ergere vormen aan als alleen wordt gekeken naar het aantal dagelijkse besmettingen en doden en de onhoudbare druk op de totale gezondheidszorg. Het wetsontwerp heeft dan ook tot doel om die bereidwilligheid voor de vaccinatie tegen het SARS-COV-2 virus op te voeren en daarmee de verspreiding en de gevolgen ervan tot een minimum te kunnen beperken.

(2). Uitgangspunten WHO en ILO

<u>World Health Organization (WHO)</u>
Het uitgangspunt van de WHO is dat vaccins een van de meest effectieve instrumenten zijn om mensen tegen COVID-192021[1] te beschermen. Met COVID-19-vaccinatie in veel landen in opmars kunnen sommige landen overwegen of zij misschien COVID-19-vaccinatie verplicht moeten stellen om de vaccinatiegraad te verhogen en volksgezondheidsdoelen te bereiken.
De WHO constateert dat het niet ongebruikelijk is dat overheden en instituten sommige handelingen of bepaalde soorten van gedrag onderhevige stellen aan verplichte vaccinatie teneinde het welzijn van individuen of gemeenschappen te beschermen.
De WHO gaat ervan uit dat dit verplichte vaccinatiebeleid ethisch gerechtvaardigd kan zijn, aangezien het van cruciaal belang kan zijn voor de bescherming van de gezondheid en het welzijn van het publiek.
Aangezien verplichte vaccinatie kan indruisen tegen individuele burgerrechten, vrijheden en de zelfbeschikking, moet worden gestreefd naar een evenwicht tussen gemeenschappelijk welzijn en individuele vrijheden. De WHO benadrukt dat, indien vaccinatiebeleid indruist tegen een

[1] COVID-19 and mandatory vaccination: Ethical considerations and caveats Policy brief d.d. 13 April 2021

individuele vrijheid, dit op zichzelf niet betekent dat dit beleid ongerechtvaardigd is. De rechtvaardiging moet hierin zijn gelegen dat het beleid dient ter bevordering van een ander waardevol sociaal doel, zoals het beschermen van de openbare gezondheid.

"Verplichte vaccinatie" (*mandatory vaccination* of *vaccintaion mandate*) komt doorgaans neer op het opleggen van **directe of indirecte dreiging** met het opleggen van beperkingen in gevallen van niet-vaccinatie. Doorgaans staat het verplichte vaccinatiebeleid een beperkt aantal uitzonderingen toe die worden erkend door autoriteiten (bijv. medische contra-indicaties die vaccineren in de weg staan). Verplichte vaccinatie gaat doorgaans niet gepaard met het daadwerkelijk dwingen of dreiging met strafrechtelijke sancties bij niet-naleving.
Toch beperkt het beleid van "verplichte vaccinatie" de individuele keuze van de persoon door vaccinatie een voorwaarde te maken voor bijvoorbeeld schoolbezoek of om te werken of de werkplaats te bezoeken in bepaalde bedrijfstakken of omgevingen, zoals de gezondheidszorg, het onderwijs of het leger.
Zo een beleid is niet ongebruikelijk constateert de WHO, hoewel moet worden opgemerkt dat de Wereldgezondheidsorganisatie (WHO) aanbeveelt om aan informatiecampagnes te werken om de burgers te motiveren om zich te vaccineren en het zoveel mogelijk toegankelijk maken van vaccins voor de bevolking. Dit zal dan ook steeds de richting zijn die door de overheid wordt gevolgd om naast de "verplichte" vaccinatie de burgerij maximaal te informeren en motiveren om zich te laten vaccineren.

De volgende overwegingen en kanttekeningen moeten in acht worden genomen door overheden en instanties die willen overgaan tot het toestaan van het verplichten van de COVID-19-vaccinatie:
1. de noodzaak van de vaccinatie en de proportionaliteit (verhoging van het middel van de vaccinatie tot het te bereiken doel);
2. voldoende bewijs van vaccinatieveiligheid;
3. voldoende bewijs van werkzaamheid en de effectiviteit van het vaccin;
4. voldoende aanbod;
5. vertrouwen van de populatie;
6. ethische besluitvormingsprocessen, waarbij alle partijen worden gehoord.

<u>International Labour Organization (ILO)</u>
De ILO zelf geeft aan dat haar verdragen en aanbevelingen niet direct ingaan op de kwestie van verplichte vaccinaties als arbeidsvoorwaarde. De ILO gaat er in haar recente *guidelines* uitgebracht door het '*Committee of Experts*' wel van uit dat op het gebied van veiligheid en gezondheid op het werk, onder de beschermende maatregelen waartoe werkgevers verplicht zijn, ook vaccinaties kunnen vallen[2].
ILO Conventie no. 155 (*Occupational Safety and Health Convention, 1981*) en ILO Conventie No. 187 (*Promotional Framework for Occupational Safety and Health Convention, 2006*) vereisen hiervoor wel specifieke samenwerking tussen management en werknemers (de bond) op het ondernemingsniveau.

[2] *ILO Standards and COVID-19, Key provisions of international labour standards relevant to the COVID-19 pandemic and recovery, and guidance from the Committee of Experts on the Application of Conventions and Recommendations*, p. 29 en 30

Hoewel werkgevers een algemene verplichting hebben om ervoor te zorgen dat de werkplekken veilig zijn, is overleg met werknemers over alle aspecten van veiligheid, gezondheid en welzijn een essentieel element voor de besluitvorming. De samenwerking is van cruciaal belang voor de uitvoering van werkplek-gerelateerde preventiemaatregelen.

De ILO geeft aan dat zij vaccinaties eerder benadert als een recht van de werknemers dan als een plicht, zoals geregeld in de ILO Aanbeveling No. 157 voor verpleegkundig personeel (*Nursing Personnel Recommendation, 1977*). Die bepaalt dat in immunisatie moet worden voorzien met betrekking tot verplegend personeel dat regelmatig aan speciale risico's wordt blootgesteld.
ILO Aanbeveling No. 171 met betrekking tot arbeidsomstandigheden (*Occupational Health Services Recommendation, 1985*) stelt dat bedrijfsgeneeskundige diensten, waar mogelijk en passend, immunisaties zouden kunnen uitvoeren met betrekking tot biologische gevaren in de werkomgeving.

De ILO bepaalt in haar bovengenoemde *guidelines* dat, indien (op basis van specifieke omstandigheden van het specifieke beroep of de sector), een besluit over verplichte vaccinatie wordt genomen door de werkgever, deze op niet-discriminerende wijze dient te worden uitgevoerd, in overeenstemming met de vereisten van Conventie No. 111 (*Discrimination (Employment and. Occupation) Convention, 1958*), en met inachtneming van specifieke omstandigheden met inbegrip van vrijstellingen.
Uit het bovenstaande blijkt dus dat de ILO een vaccinatie vanuit de werkgever niet zonder meer uitsluit, maar het is in casu sector- en werkplek-gebonden.

(3). Grondrechtelijke aspecten

De bestrijding van de epidemie heeft de overheid in de afgelopen periode genoodzaakt tot het treffen van ingrijpende maatregelen ter bescherming van de volksgezondheid. Ook op het moment van indiening van dit wetsvoorstel gelden er enkele vrijheidsbeperkende maatregelen. Gelet op de Grondwet en internationale mensenrechtenverdragen is het noodzakelijk om voor eventuele maatregelen die raken aan grondrechten een formele wettelijke basis te creëren, waarbij ook uitdrukkelijk inhoudelijke criteria worden opgenomen om voorzienbaar te maken welke maatregelen kunnen worden getroffen.
De noodzaak van overheidsoptreden ter bestrijding van de epidemie vloeit mede voort uit het recht op gezondheidszorg als mensenrecht. De Grondwet waarborgt dat de overheid maatregelen treft ter bevordering en bescherming van de volksgezondheid. De strekking van dit sociaal grondrecht komt overeen met hetgeen in internationale verdragen is bepaald. Zo brengt bijvoorbeeld artikel 12 van het Internationaal verdrag inzake economische en sociale en culturele rechten (IVESCR) mee dat het recht op een zo goed mogelijke lichamelijke en geestelijke gezondheid wordt erkend door de overheid en dat ter volledige verwezenlijking van dat recht maatregelen worden genomen, zoals maatregelen ter voorkoming, behandeling en bestrijding van epidemische en endemische ziekten alsmede van beroepsziekten en andere ziekten.
Overheidsmaatregelen ten behoeve van de (volks)gezondheid kunnen raken aan grondrechten, zoals het privéleven of bewegingsvrijheid. Als de maatregelen een beperking inhouden van vrijheidsrechten, dan moeten de maatregelen voldoen aan de zogenoemde beperkingsclausules, waarin de meeste van deze vrijheidsrechten voorzien.

Maatregelen kunnen slechts worden ingezet als zij een legitiem doel dienen. De bescherming van de volksgezondheid wordt bij een aantal grondrechten expliciet als doelcriterium genoemd. De maatregelen alsook de wettelijke basis dienen een legitieme doel en zal steeds kenbaar en voorzienbaar moeten zijn. Het is voorts proportioneel en in overeenstemming met het subsidiariteitsvereiste. Deze wet biedt de grondslag daartoe alsmede ten aanzien van de bij presidentieel besluit te treffen regelingen. Deze maatregelen kunnen worden getroffen ter bescherming van de (volks)gezondheid als legitiem doel, nu er sprake is van een epidemie van een infectieziekte. De specifiek te treffen maatregelen zijn noodzakelijk, waarbij sprake is van een dringend maatschappelijk belang en de vereiste proportionaliteit in acht wordt genomen.
Ten slotte dient er steeds een adequaat rechtsmiddel open te staan. Het type rechtsmiddel dat openstaat voor de maatregelen, waarin dit wetsvoorstel voorziet, is afhankelijk van het gebruikte handhavingsinstrument dan wel de opgelegde sanctie (bestuurlijk dan wel strafrechtelijk).

(4). Rechtspraak

Gelet op het vonnis van Stutgard/Donk vs de Staat Suriname (24 maart 2021; AR no. 210733) alsmede het vonnis van de Rechtbank Den Haag (06 oktober 2021; nr. C-09-618078-KG ZA 21-892) is het wel cruciaal dat de Regering als initiatiefnemer van de wet afgaat (en voortbouwende wetgevende handelingen pleegt) op basis van de noodzaak van de wettelijke maatregel vastgesteld door een gezondheidsautoriteit. Dat kan zijn de minister van Volksgezondheid, de Surinaamse ‘surgeon general’, het BOG of het Outbreak Management Team.
De Surinaamse kantonrechter ging gelet op de stand van de wetgeving en Nederlandse rechtspraak die in Suriname een goed toetsingskader kan zijn, voor zichzelf het volgende toetsingskader bij de beoordeling (van de eis of de regering te ver was gegaan in het beperken van grondrechten van burgers middels het bevelen van het dragen van de mond- en neusbedekking):

1. Er moet sprake zijn van buitengewone omstandigheden. Daarvan was in casu wel sprake volgens de rechter;
2. De beginselen van proportionaliteit en subsidiariteit moeten in acht worden genomen bij het doorvoeren van maatregelen waarbij grondrechten worden beperkt. Ten aanzien van de proportionaliteit was de rechter van oordeel dat de regering op het advies van het Outbreak Management Team (OMT) mocht afgaan;
3. Dat de vraag welke maatregelen moeten worden getroffen ter bestrijding van de coronacrisis en of die proportioneel en subsidiair worden getroffen, primair moeten worden beantwoord door de regering en de wetgevende macht (en dat de rechter zich terughoudend opstelt met betrekking tot de beoordeling van alzo gemaakte keuzes). Er ontstaat ruimte voor rechterlijk ingrijpen als het evident is dat bij de beperking van de grondrechten onjuiste keuzes zijn gemaakt, dus men in redelijkheid niet voor het gevoerde beleid heeft kunnen kiezen.

In verschillende vonnissen en naar het oordeel van het Nederlandse College Rechten van de Mens, mogen de grondrechten die hier aan de orde zijn, tijdelijk bij wet worden beperkt, onder zekere voorwaarden.

(5). Artikelsgewijs

Er is voor gekozen om de maatregelen in het kader van de verplichte vaccinatie voor de toegang tot voor het publiek toegankelijke plaatsen en specifieke besloten plaatsen in het nieuw artikel 6a van de Wet Uitvoering Burgerlijke Uitzonderingstoestand op te nemen, gelet op het tijdelijke

karakter dat aan deze maatregel wordt gegeven.
Het zal slechts gedurende de afkondiging van de COVID-19 Uitzonderingstoestand van kracht zijn (artikel 6a lid 1). In dit zelfde kader is daarom ook niet gekozen voor een algemene vaccinatieplicht (rechtstreekse verplichting voor een ieder), zoals dat het geval is ten aanzien van een aantal ziekten ingevolge het Vaccinatie Decreet 1982 (S.B. 1983 no. 21).

In ARTIKEL I onder A is een nieuw onderdeel g toegevoegd, luidende: besloten plaats.
Een besloten plaats, niet zijnde een woning is een niet voor een ieder toegankelijke plaats, zoals een erf of loods. Ook fabrieks- of bedrijfsruimten vallen niet onder het begrip 'woning' (zie in dit kader de Toelichting van art 126k Nederlandse Strafvordering in de literatuur, Tekst en Commentaar, C.P.M. Cleiren en J.F. Nijboer, 8e druk).
De jurisdictie van de Arbeidsinspectie is echter niet beperkt tot woningen en kunnen die, indien er indicaties zijn dat daar arbeid wordt verricht, ook worden betreden, weliswaar onder enige in de Wet Arbeidsinspectie (S.B. 1983 no. 42, zoals gewijzigd bij S.B. 2017 no. 39) genoemde voorwaarden. De bijzondere maatregelen met betrekking tot de vaccinatie zullen gelden op de werkplekken die tegelijkertijd woningen zijn. Hier valt te denken aan de in ILO Conventie No. 190 genoemde 'domestic workers' oftewel huishoudelijke werknemers die in gelijke mate dienen te worden beschermd.

Onder B is een nieuw artikel 6a toegevoegd, waarin maatregelen zijn opgenomen specifiek gericht op de bestrijding van COVID-19.
Ingevolge artikel 6a lid 2 worden bij presidentieel besluit de voor het publiek toegankelijke en besloten plaatsen aangewezen, waarbij voor de toegang of om aldaar aanwezig te zijn, voldaan dienen te worden aan de in dat presidentieel besluit gestelde voorwaarden.
Het betreft die plaatsen waar personen bij elkaar zijn, waarbij kennelijk sprake is van een zekere samenhang of omstandigheid.
In artikel 6a lid 2 zijn, ten aanzien van de aan te wijzen plaatsen in ieder geval genoemd plaatsen waar arbeid wordt verricht of pleegt te worden verricht of ten aanzien waarvan redelijkerwijze kan worden vermoed dat aldaar arbeid wordt verricht. Deze plaatsen kunnen een publieke, maar ook een besloten karakter hebben of een combinatie daarvan, en zijn, gelet op hun karakter bij uitstek de plaats waarbij personen gedurende een bepaalde tijd bij elkaar zijn en waar de kans op besmettingen erg groot aanwezig is. De overige bij presidentieel besluit aan te wijzen plaatsen zullen in het bijzonder betrekking hebben op die plaatsen, waarbij (grote) groepen van personen bij elkaar zijn, zoals evenementen.

In artikel 6a lid 3 is specifiek wettelijk vastgesteld welke voorwaarde in elk geval gesteld kan worden. Er kunnen namelijk ook andere minder ingrijpende voorwaarden worden gesteld, zoals de inachtneming van hygiënische maatregelen, die eveneens reeds een grondslag hebben in het algemeen artikel 6.
De specifiek in artikel 6a lid 3 van deze wet gestelde voorwaarde is dat voor de toegang tot de in lid 2 bedoelde plaatsen of voor het aldaar aanwezig zijn, de personen bewijs moeten kunnen leveren van volledig gevaccineerd zijn tegen SARS-COV-2 of een in dat presidentieel besluit vastgesteld door de overheid erkend SARS-COV-2 antigeen-sneltest, die niet ouder is dan 24 uur. Het voorgaande laat onverlet de mogelijkheid voor degene die niet is gevaccineerd toch de toegang tot bedoelde plaatsen te verkrijgen of om aldaar aanwezig te zijn, indien deze een negatieve SARS-

COV-2-RT PCR test of SARS-COV-2 antigeen-sneltest kan overleggen. Daarmee wordt eveneens voldaan aan het doel waarvoor deze maatregel wordt ingesteld.

Ten aanzien van voornoemde verplichting zijn in de tweede volzin van artikel 6a lid 3 uitzonderingen opgenomen. De in de eerste volzin genoemde verplichting tot overlegging van een bewijs van vaccinatie of van de daarin genoemde testen is niet van toepassing op:

a. een persoon tot en met de leeftijd van twaalf jaar of
b. een persoon waarvan wegens medische gronden vaccinatie tegen SARS-COV-2 of het uitvoeren van genoemde testen ongewenst is of achterwege behoort te blijven, zulks blijkende uit een door een medische specialist afgegeven verklaring of
c. een persoon met religieuze gewetensbezwaren.

De tot nu toe ontwikkelde en door de WHO goedgekeurde vaccins hebben betrekking op personen boven de 12 jaar.

In lid 4 is eveneens voorzien in een uitzondering, waarbij voor de toegang kan worden volstaan met een eerste vaccinatieprik, in de gevallen waarbij voor een volledige vaccinatie meer dan één keer dient te worden gevaccineerd. De toegang met de eerste vaccinatieprik is toegestaan tot de datum op de vaccinatiekaart waarop de tweede en laatste vaccinatieprik dient te zijn ontvangen. Dit dient om te voorkomen dat werknemers en anderen hun vaccinatie onvolledig laten en hun tweede tevens laatste vaccinatieprik niet halen.

In lid 5 wordt de zorgplicht tot handhaving van voornoemde verplichting eveneens gelegd in handen van degenen die ten aanzien van de aangewezen plaatsen enige verantwoordelijkheid hebben. Op de eerste plaats zijn dat de eigenaar en werkgever.
De werkgever, de eigenaar of het hoofd of de bestuurder en het opzichthoudend personeel of degene die verantwoordelijk is voor de in lid 2 bedoelde plaatsen of die bevoegd is tot het treffen van voorzieningen met betrekking tot de toegang daartoe, draagt zorg dat de personen aan wie toegang worden verleend tot die plaatsen of om aldaar aanwezig te zijn, voldoen aan de krachtens de leden 2 en 3 gestelde voorwaarden.

Benadrukt dient te worden dat de handhavingsbepalingen en sancties ingevolge de artikelen 9 e.v. van toepassing zijn (zie onderdeel C).

Paramaribo, de ……

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PRODUKTIE 11

THE LIGHT

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How the world was conned

Review of the film *The Viral Delusion*, PAGE 6

Pfizer knew their vaccine would kill

Own data show shocking number of fatalities and side effects now officially associated with covid shots

by **JANINE GRIFFITHS**

THE documents were first leaked in a cyber attack on the European Medicines Agency website. More than 40 megabytes of classified information from the agency's review were published on the dark web, and several journalists including those at the British Medical Journal were sent copies of the leak.

In the U.S., the Food and Drug Administration had previously agreed to withhold the documents and their jaw-dropping revelations from the public for 75 years, until Texas District Judge Mark Pittman ordered their release within eight months, stating it was 'of paramount public importance'.

Most alarmingly of all, the documents show that in the trials there were at least 1,223 deaths reported in the first 28 days after injection.

The NHS, media and the government continually state that the vaccines are 'safe and effective' while those that report vaccine-related injuries via the Yellow Card scheme are often accused of making false correlations or imagining their symptoms.

However, the Pfizer documents paint a very different picture, listing thousands of side effects that occurred at an alarming rate, which were as a direct result of taking the experimental genetic injection.

According to their report, Pfizer hired 600 extra staff to handle the sheer number of adverse reactions from its covid-19 shot, and said it had planned to hire 1,800 in total.

Serious side effects included, but were not limited to: auto-immune disorders; blindness; diabetes; herpes; heart problems such as myocarditis; thyroid disorders; neurological conditions such as multiple sclerosis; seizures; epilepsy; narcolepsy and Guillain-Barré Syndrome.

Non-fatal conditions such as eczema, blisters, asthma, fertility problems, inflammatory bowel disease, deafness and even tongue biting are also listed among the side effects by Pfizer.

While it has been approved for use in pregnant women, it is also known to cause pregnancy complications, including many spontaneous abortions. One of the many issues it causes is anaphylactoid syndrome of pregnancy or ASP for short.

ASP is a fatal disease for mothers and is among the leading causes of maternal mortality. Symptoms include severe bleeding, confusion, shortness of breath and anxiety. There is therefore a high risk for pregnant women taking the covid 'vaccine'.

The Pfizer document also lists various blood disorders, Crohn's disease and liver failure as side effects. Blood clotting was another issue reported from the trials.

One of the most telling side effects listed is… covid-19. Proponents often argue that despite the possible side effects associated with some of the covid shots, they at least prevent people from dying from covid-19.

The problem is that the 'vaccine' actually causes people to develop the disease, and so it is contributing to the number of cases, listing covid-19-associated pneumonia as a side effect.

Some may argue that these problems are only associated with the Pfizer shot, but death and serious injuries have been present and publicly acknowledged with all of the manufacturers' injections.

Research developed by Edinburgh University showed that almost 350 Britons have been struck down with a rare clotting disorder after getting the AstraZeneca vaccine.

These blood clots cause minor bruising around the body and can leave some with a purple-dotted rash.

The Moderna vaccine has been associated with heart problems such as myocarditis and pericarditis. Their list of adverse reactions also includes inflammation, fainting and breathing difficulties.

Data from the UK Health Security Agency (UKHSA) in the table on page 2 has also revealed that both covid-19 deaths and cases were worse in vaccinated people, particularly those over the age of 18. The official data is clear: the chances of developing covid-19 increases significantly following subsequent 'booster' jabs.

This is broadly in line with the information contained in the Pfizer document, which states that the shots cause covid-19 and respiratory illnesses.

Coupled with the fact that ONS data recently revealed that covid deaths were much lower than previously thought, the risks of taking the vaccine seem to greatly outweigh the risks of not doing so.

For sources please see page 2

Janine Griffiths is founder and editor of akashictimes.co.uk

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"The world is a business, Mr. Beale."
- Network 1976

<<< Continued from page 1

Pfizer vaccines kill - references

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Table 10. COVID-19 cases by vaccination status between week 5 2022 and week 8 2022
Please note that corresponding rates by vaccination status can be found in Table 13.

Cases reported by specimen date between week 5 2022 (w/e 6 February 2022) and week 8 2022 (w/e 27 February 2022)	Total	Unlinked*	Not vaccinated	Received one dose (1 to 20 days before specimen date)	Received one dose, ≥21 days before specimen date	Second dose ≥14 days before specimen date[1]	Third dose ≥14 days before specimen date[1]
	[This data should be interpreted with caution. See information below in footnote about the correct interpretation of these figures]						
Under 18	244,403	11,642	169,482	2,588	40,627	18,961	1,103
18 to 29	197,577	15,845	27,313	816	10,460	54,092	89,051
30 to 39	210,906	12,215	24,469	420	6,525	44,602	122,675
40 to 49	187,850	8,738	13,228	197	3,261	25,954	136,472
50 to 59	144,909	6,562	5,871	81	1,417	12,030	118,948
60 to 69	86,258	3,890	2,263	36	617	4,051	75,401
70 to 79	50,250	2,188	932	19	302	1,501	45,308
80 or over	32,706	2,850	755	7	296	1,807	26,991

* Individuals whose NHS numbers were unavailable to link to the NIMS.

Problems with Moderna vaccine:

- https://www.marketwatch.com/story/blood-clots-as-prevalent-with-pfizer-and-moderna-vaccine-as-with-astrazenecas-report-2021-04-15
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MHRA LATEST

GOV.UK

MHRA Yellow Card Reporting

2,075
DEATHS

1,475,298
ADVERSE REACTIONS

Data correct as of:
24/03/2022

Search 'summary of yellow card reporting' - on the UK government's website, scroll down to the bottom of annex 1 and click the print analysis for each 'vaccine' maker. Reports are made by patients or their doctors but it is estimated that only around 5-10% of all reactions are reported.

THIS IS A NATIONAL SCANDAL. COVID 'VACCINES' ARE KILLING AND INJURING PEOPLE, AND IT IS BEING SWEPT UNDER THE CARPET BY GOVERNMENT AND MEDIA.

Artwork: bobmoran.co.uk

DE ANDERE KRANT | 14-21 DEC 2022

mRNA-vaccins komen steeds meer onder vuur te liggen

Fotografie: Mike Marsen

80.000 pagina's aan geopenbaarde documenten van vaccinfabrikant Pfizer leveren aardig wat narigheid op. 1223 van de 42.086 proefpersonen overleden binnen vier weken na toediening van het Pfizer-'vaccin'. Ook de effectiviteit van de Pfizer- en Moderna-injecties valt tegen.

Huib Rutten

De Pfizer-studie liet daarnaast duizenden – ook zeer ernstige – bijwerkingen zien. Ook blijkt dat het Pfizer-'vaccin' slechts 12-15 procent effectief was in het voorkomen van infectie in het algemeen. Dat percentage daalde al snel tot minder dan 1 procent – ondanks dat politici en gezondheidsfunctionarissen beweerden dat de effectiviteit minstens 90 procent zou zijn.

Ze logen dus, maar hierover, en over de zorgwekkende resultaten, zwijgt het kabinet in Den Haag. Evenmin laten artsenberoepsgroepen zich hierover uit. Dit

Placebo scoort beter

Moderna kwam onlangs ook in het nieuws met onderzoeksgegevens die ze al anderhalf jaar bezitten. Het Moderna-'vaccin' (net als die van Pfizer, AstraZeneca en Janssen) is slechts gericht op één virus-eiwit, namelijk het spike-eiwit. Het Sars-Cov-2 virus bestaat echter uit nog een aantal eiwitten en bij infectie maakt het immuunsysteem dan ook antistoffen tegen al die verschillende eiwitten. Er werd onderzocht wat het effect was op één ander belangrijk eiwit (anti-N) na een infectie. Het betrof een studie waarbij placebo met Moderna vergeleken werd. Belangrijkste bevindingen waren dat ná vaccinatie met Moderna maar 40 procent dan zal het voor het virus moeilijker zijn immuunvluchteigenschappen te ontwikkelen zoals die van omikron, die in wezen de immuniteit ontwijkt[2].

Statistische illusie

Toch blijven beleidsmakers en veel medici naar het succes van de vaccins wijzen. Echter, systeemfouten of vooroordelen kunnen leiden tot conclusies die het omgekeerde van de werkelijkheid zijn. Bijvoorbeeld: het simpelweg een week te laat melden van sterfgevallen wanneer een vaccinprogramma wordt uitgerold zal (met statistische zekerheid) leiden tot succes van elk vaccin, zelfs een placebo, om de mortaliteit schijnbaar te verminderen.

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Duitse verzekerings-maatschappij: "tienduizenden overlijdens door vaccinaties"

Van onze redacteur

Het aantal overlijdens en ernstige schadegevallen als gevolg van de coronavaccinaties in Duitsland is vele malen hoger dan uit officiële cijfers blijkt. Dat stelt Andreas Schöfbeck, bestuurslid van de Duitse verzekeringsmaatschappij BBK dat 10,9 miljoen verzekerden als klant heeft, in een interview met het Duitse dagblad Die Welt. Schöfbeck heeft een brief gestuurd aan het Paul Ehrlich Institut (PEI) dat in Duitsland de bijwerkingen van de vaccinaties registreert. Het PEI meldde tot dusver 38 bijwerkingen per 100.000 gevaccineerden. In Nederland ligt dat cijfer op 701.

"Onethisch om gegevens niet naar buiten te brengen"

Volgens Schöfbeck zijn de werkelijke cijfers in Duitsland veel hoger. Op grond van de gegevens onder haar verzekerden, stelt BKK dat er 216.695 bijwerkingen zijn gemeld waarbij behandeling door een arts nodig was. Geëxtrapoleerd naar de hele bevolking gaat het om 2,5 tot 3 miljoen mensen die behandeling nodig hebben gehad. Daarbij gaat het om 31.000 mensen die zijn overleden en 412.000 die zware bijwerkingen hebben ondervonden, waarvoor ze naar het ziekenhuis moesten. Schöfbeck noemt de gegevens een "alarmsignaal". Het zou "onethisch zijn om ze niet naar buiten te brengen", zei hij tegen Die Welt. ■

Bundesamt
für Bevölkerungsschutz
und Katastrophenhilfe

PRODUKTIE 12

Onderwerpen | Justitie en politie | Nieuws uit Suriname | Uitgelicht

Man dood neergevallen aan de Zonnebloemstraat

11 april 2022 2

Aan de Zonnebloemstraat in Suriname is een man vanmorgen dood neergevallen. Dit gebeurde rond 11.00u voor de Maria Hartmannschool.

De man lag roerloos deels uit zijn voertuig, deels op het trottoir. Hij werd door omstanders uit het voertuig gehaald en op de grond geplaatst.

Een ambulance van het Academisch Ziekenhuis werd ingeschakeld. Bij aankomst werd door het ambulancepersoneel geconstateerd dat de man geen teken van leven meer vertoonde.

Onderwerpen | Justitie en politie | Nieuws uit Suriname | Uitgelicht

54-jarige man valt dood neer tijdens maaiwerkzaamheden

20 juni 2022 2

De 54-jarige Randolf De Vries is zondag tijdens maaiwerkzaamheden, plotseling dood neergevallen. Dit gebeurde aan de Abigaellustweg in Suriname.

De Vries was bezig te maaien met een brushcutter, toen hij bewusteloos neerviel. Er werd een ambulance ingeschakeld en het personeel dat ter plaatse arriveerde, merkte dat de man geen polsslag meer had.

Een arts stelde de dood officieel vast. Volgens de arts heeft het slachtoffer vermoedelijk een hartstilstand gekregen. Na afstemming met het Surinaamse Openbaar Ministerie is het ontzielde lichaam afgestaan aan de nabestaanden.

Onderwerpen | Justitie en politie | Nieuws uit Suriname | Uitgelicht

Taxichauffeur overleden in eigen auto; doodsoorzaak nog onbekend

11 april 2022 1

Een 47-jarige taxichauffeur is afgelopen nacht rond 04.15u in zijn eigen voertuig overleden. Dit gebeurde aan de Tajerbladstraat in Suriname.

De man genaamd Jerry S., werd in z'n auto aangetroffen door enkele bezoekers van een bar, die op zoek waren naar een taxi. Ze liepen naar de auto en dachten in eerste instantie dat de man in het voertuig sliep.

Ze tikten op de autoruit en ontdekten dat de taxichauffeur in ademnood verkeerde. Ze sloegen gauw een van de autoruiten stuk om de man te redden, maar het bleek dat de taxichauffeur zijn laatste adem had uitgeblazen. Hij overleed ter plaatse.

Onderwerpen | Justitie en politie | Nieuws uit Suriname | Uitgelicht

Vrouw raakt onwel in bus en komt te overlijden

11 april 2022 5

De ambulance werd ingeschakeld door de politie.

Een 64-jarige vrouw is deze ochtend plotseling overleden in het centrum van Paramaribo. Dit gebeurde vanmorgen rond 09.30u aan de Keizerstraat in Suriname.

De redactie van Waterkant.Net verneemt dat de vrouw genaamd Shirley J.L. in een bus zat toen ze ineens onwel werd. Ze raakte bewusteloos waarna de buschauffeur zijn voertuig aan de kant parkeerde en de politie inschakelde.

Nadat een ambulance werd ingeschakeld werd de vrouw in de ziekenwagen geplaatst. Het ambulancepersoneel stelde echter vast dat ze geen teken van leven vertoonde. Een arts werd ingeschakeld en stelde de dood vast.

Onderwerpen | Justitie en politie | Nieuws uit Suriname | Uitgelicht

Bewusteloos geraakte man dood binnengebracht bij SEH

7 juli 2022 3

Een 54-jarige man, die woensdagmorgen bewusteloos neerviel aan de Tesimistraat in Suriname, is kort daarna dood binnengebracht bij de Spoedeisende Hulp (SEH).

Op die bewuste morgen viel de man genaamd Hazratali Hausil bewusteloos neer aan bovengenoemde straat te Kasabaholo. De ingeschakelde politie van Uitvlugt, die ter plaatse ging voor onderzoek, trof betrokkene aan.

Hij kwam weer bij, maar weigerde met de ambulance afgevoerd te worden en ging daarbij te keer. Plotseling verkeerde de man in ademnood en werd hij toch met de ambulance vervoerd. Onderweg naar de SEH gaf hij de geest.

Onderwerpen | Justitie en politie | Nieuws uit Suriname | Uitgelicht

31-jarige man valt plotseling dood neer: lichaam in beslag genomen

27 juli 2022 1

Een 31-jarige man is dinsdagavond plotseling overleden in een woning aan de Dr. Redmondstraat in Suriname. Vernomen wordt, dat hij samen met een paar vrienden zat te borrelen.

Op een gegeven moment stond hij op en liep naar een bank om te gaan liggen. Iets later trof men hem roerloos op de grond op balkon aan. Hij vertoonde geen tekenen van leven meer.

De politie van Centrum werd ingeschakeld, die op haar beurt een arts ingeschakelde om de dood officieel vast te stellen. De arts twijfelde over de doodsoorzaak.

WATERKANT NIEUWS VIDEO NIEUWS OTHER ENTERTAINMEN

Home › Onderwerpen › Justitie en politie › Man overleden in DNV-gebouw

Onderwerpen | Justitie en politie | Nieuws uit Suriname | Uitgelicht

Man overleden in DNV-gebouw

26 juli 2022 0

Deel

Een 56-jarige man is hedenmorgen overleden in het gebouw van het Directoraat Nationale Veiligheid aan de Grote Combéweg in Suriname.

Vernomen wordt, dat de overledene een supervisor was bij een security bedrijf. Hij reed vanmorgen over de Grote Combéweg, toen hij zich plotseling niet goed voelde. De man parkeerde zijn voertuig aan de kant en vroeg aan één van de medewerkers van het Directoraat Nationale Veiligheid om hulp.

Een DNV-er bracht het slachtoffer naar het gebouw en vervolgens naar het toilet in het gebouw van het DNV. Nadat de medewerker niets meer hoorde stelde hij een onderzoek. Het bleek dat de man in het toilet was gevallen en geen teken van leven meer vertoonde.

THE IRISH LIGHT

Issue 11

People-Funded Paper

FREE

The Government is coming for your home

John Waters on why we must resist the attack on property rights: p10

Heart disease in children explodes since vaccine

Sudden deaths of children soar as media stay silent

THE greatest crime ever committed by an Irish government - and there have been many - will not be concealed from the Irish people much longer. As hard as HSE tries to cover up the driving impact of the covid jab on Irish children, there is containing the staggering sudden deaths in young

...ly, the faces of sporty ...d newborn infants appear ... of RIP's: perfectly ...ldren struck down by a ...t attack, stroke or sudden ...ed death.

...has also been a sharp rise in ...dden and severe hepatitis ...ion of the liver) in children ...hich has been seen in at ...ntries including Ireland. ...so many healthy children ...has changed in their lives. ...e all know the answer but ...ot have the courage to ... because they know they ...he same fate.

...diologist Dr Peter ...ke recently about the ...of concern and outrage ...ly members when ...after the vaccine. He ...mass psychosis that ...pen since the advent ... that these people ...state where they ...to the death of a ...has been caused ...le.

...f cognitive dissonance and denial often witnessed in parents whose perfectly healthy toddler becomes violently autistic in the aftermath of the MMR vaccine. They know what changed their child overnight but cannot state it publicly because they are the ones responsible.

And so it is with the covid vaccine: how many children whose lives have been wiped out were urged to take it by their reckless parents? They will have to live with that for the rest of their lives. If only they knew the peace and strength they would feel if they could find the courage to speak out and save other young lives. At least their child's death would not have been in vain.

But soon the dam of silence will burst because the injury levels are too alarming to ignore.

In the US, the number of injuries and deaths recorded in the government database of Vaccine Adverse Events Reporting System (VAERS) following covid vaccines has soared above 1.2 million cases.

This represents an increase of 3008% compared to the previous 30 years of vaccine use.

In the world of sport, there has been at least 930 post-vaccine heart attacks and more than 620 deaths.

As of March 24, 2022, VAERS had received 2,323 reports of heart inflammation among people ages 30 years and younger who received the vaccine.

Youngsters involved in the GAA - which took a draconian approach to vaccination - have been dying at a terrifying rate.

RTE and the rest of the mainstream media, which could not exist without Big Pharma/HSE funding, should be interrogating the sporting organisation as to why so many of its young members are dropping dead. But instead they close ranks refusing to even acknowledge the sheer numbers who are dying and try to normalise sudden death, heart disease and strokes in children or cynically imply that the child committed suicide.

It is a crime which will seal their demise when the public finally learn the truth about how they were duped into taking this lethal experimental drug.

Even the manufacturers admit in the small print that their vaccines have side effects.

Pfizer released a document listing over 9 pages of over 1200 adverse events of special interest.

Continued on page 2 >>>

Zeer zeldzaam

Lareb: 373 meldingen van hartontstekingen na coronavaccins

02 mei 2022 15:39

De bijwerkingen kwamen vooral voor bij [illegible] boven de 40.

Bijwerkingencentrum Lareb heeft tot eind januari 373 meldingen ontvangen van een ontsteking van de hartspier (myocarditis) of het hartzakje (pericarditis) na coronavaccinatie. Dat zijn er 142 meer dan bij de vorige rapportage eind november vorig jaar.

In Nederland zijn meer dan 30 miljoen vaccins gezet bij ruim 12 miljoen mensen. De meeste bijwerkingen zijn zeldzaam, en Lareb wijst erop dat de hartontstekingen 'bekende zeldzame bijwerkingen' zijn van de vaccins van Pfizer/BioNTech en Moderna.

Myocarditis kwam vooral voor bij mannen jonger dan 40 jaar. Ook pericarditis is vooral gemeld bij mannen. Het ging hierbij ook om ouderen.

Lees ook:

In jaar tijd 36 nieuwe bijwerkingen coronavaccins ontdekt: 'Hier blijft het wel bij'

(https://www.rtlnieuws.nl/nieuws/artikel/5266027/vaccins-corona-covid-19-bijwerkingen)
Volgens het centrum zijn er drie mensen overleden aan hartproblemen na myocarditis of pericarditis, na vaccinatie met Pfizer/BioNTech. "In deze meldingen kunnen ook infecties of andere hartaandoeningen een rol hebben gespeeld. Dat myocarditis of pericarditis na vaccinatie optreedt, betekent niet dat het vaccin altijd de oorzaak is", benadrukt Lareb.

Drie mensen overleden

Twee mensen overleden na een hartontsteking na een prik met het Janssen-vaccin en één na inenting met AstraZeneca. "Van deze vaccins zijn dit geen bekende bijwerkingen", zegt het bijwerkingencentrum.

Van het totale aantal meldingen gaat het in 274 van de gevallen om pericarditis en 99 keer om myocarditis. Lareb geeft daarbij aan dat uit onderzoeken blijkt dat het risico op myocarditis en pericarditis door Covid groter is dan door de coronavaccins.

Lees ook:

Wat is het verschil tussen gewone trombose en trombose door een coronavaccin?

(https://www.rtlnieuws.nl/nieuws/nederland/artikel/5226215/corona-update-coronavaccin-covid-19-trombose-astrazeneca-janssen)
"Artsen en mensen die gevaccineerd zijn, moeten goed letten op klachten zoals kortademigheid, pijn op de borst en onregelmatige hartslag, die kunnen wijzen op myocarditis of pericarditis. Wie deze klachten heeft, moet contact opnemen met een arts. De klachten gaan meestal vanzelf over of zijn met medicijnen goed te behandelen", zegt de organisatie.

Trombosegevallen

Lareb ontving verder 2080 meldingen van trombose en embolieën, een bloedprop in een bloedvat, na coronavaccinaties. Trombose en longembolie komen ook los van vaccinatie voor, onderstreept het centrum. Lareb is in samenwerking met het Leids Universitair Medisch Centrum (LUMC) een vervolgonderzoek gestart naar het risico op trombose na coronavaccinatie.

Ook maakte Lareb bekend dat er tot dusver 683 meldingen zijn gedaan van overlijden na een coronaprik. Dat betekent volgens het centrum niet dat een bijwerking van het vaccin de oorzaak is van het overlijden.

Bekijk ook: Waarom het (nog) niet lukt de hele wereld tegen corona te vaccineren

[redacted]

June 3, 2022
6:13 PM UTC
Last Updated a day ago

Future of Health

U.S. FDA flags risk of heart inflammation after Novavax COVID vaccine

By Manas Mishra and Mrinalika Roy

3 minute read

1/2 A vial labelled "Novavax COVID-19 Vaccine" is seen in this illustration taken January 16, 2022. REUTERS/Dado Ruvic/Illustration

June 3 (Reuters) - The U.S. Food and Drug Administration hasraised concerns about a possible risk of heart inflammation from Novavax Inc's (NVAX.O)COVID-19 vaccine, even as the company's data showed it could reduce the chances of mild-to-severe disease.

In Novavax's nearly 30,000 patient trial, conducted

Register

In Novavax's nearly 30,000 patient trial, conducted between December 2020 and September 2021, there were four cases of a type of heart inflammation calledmyocarditis detected within 20 days of taking the protein-based shot.

"These events raise the concern for a causal association with this vaccine, similar to the association documented with mRNA COVID-19 vaccines," FDA staff wrote in briefing documents released on Friday.

Shares of the company fell nearly 14% after the FDA's analysis of data from the company's trial.

The agency said it had requested Novavax to flag myocarditis and another kind of heart inflammation called pericarditis as an "important identified risk" in its materials. The company has not yet agreed to do so.

Novavax, in response to the safety concerns flagged by the FDA, said natural background events of myocarditis can be expected in any sufficiently large database.

"Based on our interpretation of all the clinical data supporting NVX-CoV2373 ... we believe there is insufficient evidence to establish a causal relationship," the company said in a statement.

One patient in the trial reported myocarditis after receiving placebo.

Novavax has said the shot, NVX-CoV2373, will play a role in driving vaccination among those who have been hesitant to get immunized and it has started an educational effort on vaccine choices.

"Despite the wide availability of authorized or approved vaccines, the SARS-CoV-2 pandemic is not well controlled in the U.S. ... there remains a desire for vaccines that have been developed using well-understood technology platforms," it said.

The FDA analyzed data from Novavax's trial before

The FDA analyzed data from Novavax's that before the Omicron and Delta variant became the dominant strains.

"Based on the efficacy estimate in the clinical trial of this vaccine, it is more likely than not that the vaccine will provide some meaningful level of protection against COVID-19 due to Omicron, in particular against more severe disease," the FDA staff said.

The vaccine showed an efficacy of 90.4% in Novavax's study, which enrolled adults across the United States and Mexico.

The FDA's comments came in a briefing note initially prepared ahead of a May 7 meeting of the agency's outside advisers.

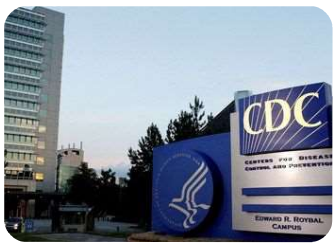
Its staff comments will be used by those advisers to guide their decision on whether or not to recommend authorizing the vaccine on Tuesday. The FDA is not mandated to follow the advise of its outside experts, but usually does.

Reporting by Manas Mishra and Mrinalika Roy in Bengaluru, and Michael Erman in New Jersey; Editing by Saumyadeb Chakrabarty, David Holmes and Devika Syamnath

Our Standards: **The Thomson Reuters Trust Principles.**

More from Reuters

Future of Health



Families open up about terrifying condition claiming lives of healthy young people

Catherine Keane was a healthy 31-year-old when she died unexpectedly in her sleep of a terrifying condition affecting young adults.

Rhiannon Lewin / Public Health / Updated 10 days ago

The family of a young Irish woman who died suddenly in her sleep are sharing their devastation and warning others of a terrifying condition affecting young adults.

Catherine Keane was a healthy 31-year-old when she died unexpectedly in her sleep last July, from a condition known as Sudden Adult Death Syndrome, or Sudden Arrhythmic Death Syndrome (SADS).

The condition is an "umbrella term to describe unexpected deaths in young people", usually under 40, when a post-mortem can find no obvious cause of death, according to the Royal Australian College of General Practitioners (RACGP).

While it's unknown how many people die of the condition globally every year, a Victorian register rolled out two years ago suggests it kills about 750 young people in that state annually.

Melbourne's Baker Heart and Diabetes Institute hopes to extend the register nationwide.

Meanwhile, Catherine's family members are sharing their story in the hopes others will get screened for SADS if there is a family history of cardiac illness.

Catherine's mother, Margherita Cummins, said her daughter was found by her flatmates last year in Dublin.

"She was living with two friends in Rathmines in Dublin, and they were all working from home, so no one really paid attention when she didn't come down for breakfast," she told the *Irish Mirror*.

"They sent her a text at 11.20am and when she didn't reply, they checked her room and found she had passed. Her friend heard a noise in her room at 3.56am and believes now that is when she died."

Catherine died suddenly in her sleep at 31 years of age. Credit: Facebook

Cummins added that Catherine was doing well at her job and was very healthy leading up to her death.

"She worked for an advertising company and was doing really well. She went to the gym and walked 10,000 steps every day," she said.

Cummins then went on to share her struggle, and said there were so many reminders of her daughter every day.

"I try and look at something positive to get me through, but there are so many reminders everywhere," she said.

"I take some comfort in that she went in her sleep and knew no pain, and I'm grateful for that. I always worried about the kids driving in the car but never saw this coming. I never thought I'd ever lose a child in my life."

Another family have also opened up about their heartache after their 19-year-old son died from SADS in April last year.

Liam, who is described as having been a "vibrant, fit and healthy young man", died from the condition suddenly, leaving his family devastated.

"Nothing could have prepared us for what happened on that day of April 2 or what potentially lay ahead of us," his mother Adele Doherty wrote on a fundraising page.

"This became our journey into a lot of uncharted waters, learning the depths of SADS, trying to understand and process it all."

Early prevention an 'important step'

While national figures are not available, Melbourne's Baker Heart and Diabetes Institute has a Victorian registry of figures, which they hope to make national.

Dr Elizabeth Paratz, cardiologist and researcher at the Institute, told 7NEWS.com.au the figures had remained consistent over the years.

"In our registry, there are approximately 750 cases per year of people aged under 50 in Victoria suddenly having their heart stop," she said.

"Of these, approximately 100 young people per year will have no cause found even after extensive investigations such as a full autopsy."

Paratz explained that the numbers had remained tragically consistent over the years.

"This has always been a really tragic thing that's been around, and we haven't seen a big change in numbers in recent years," she said.

"It's always been something that affects people in their life with no warning.

"So, if there is any family history, it is a very good idea to get a screening."

The RACGP has guidelines that recommend those who may be at risk to get screened.

It said any first-degree relatives of an individual with a genetic arrhythmogenic disorder are at a 50 per cent higher risk of developing the condition.

The RACGP says the following individuals are at risk:

- Any first-degree relatives with unexplained sudden cardiac death under 40 years of age
- Episodes of unexplained syncope (fainting)
- Syncope or seizures during exercise, excitement or startle.

A medically reviewed report on US site Healthline said most people didn't know they had the syndrome until a cardiac arrest occurred.

"Because SDS is often misdiagnosed or not diagnosed at all, it's unclear how many people have it," the report said.

It said while there was no known cure for the condition, an early diagnosis was an important step in preventing a fatal episode.

Healthy young people are dying suddenly and unexpectedly from a mysterious syndrome - as doctors seek answers through a new national register

- **People aged under the age of 40 being urged to go and get their hearts checked**
- **May potentially be at risk of having Sudden Adult Death Syndrome (SADS)**
- **SADS is an 'umbrella term to describe unexpected deaths in young people'**
- **A 31-year-old woman who died in her sleep last year may have had SADs**

By TOM HEATON FOR DAILY MAIL AUSTRALIA
PUBLISHED: 07:05 BST, 8 June 2022 | **UPDATED:** 07:32 BST, 8 June 2022

People aged under 40 are being urged to have their hearts checked because they may potentially be at risk of Sudden Adult Death Syndrome.

The syndrome, known as SADS, has been fatal for all kinds of people regardless of whether they maintain a fit and healthy lifestyle.

SADS is an 'umbrella term to describe unexpected deaths in young people', said The Royal Australian College of General Practitioners, most commonly occurring in people under 40 years of age.

People aged under 40 are being urged to have their hearts checked, because they may potentially be at risk of Sudden Adult Death Syndrome (SADS) (pictured, woman experiencing chest pain while running)

The term is used when a post-mortem cannot find an obvious cause of death.

The US-based SADS Foundation has said that over half of the 4,000 annual SADS deaths of children, teens or young adults have one of the top two warning signs present.

Those signs include a family history of a SADS diagnosis or sudden unexplained death of a family member, and fainting or seizure during exercise, or when excited or startled, reported **news.com.au**.

Last year a 31-year-old woman, Catherine Keane, died in her sleep while living with two friends in Dublin.

Catherine Keane (pictured right with her mother Margherita), 31, was found to have died in her sleep while living with two friends in Dublin last year

Her mother Margherita Cummins told the **Irish Mirror**, 'They were all working from home so no one really paid attention when Catherine didn't come down for breakfast.'

'They sent her a text at 11.20am and when she didn't reply, they checked her room and found she had passed.

'Her friend heard a noise in her room at 3.56am and believes now that is when she died.'

Ms Cummins stated that her daughter 'went to the gym and walked 10,000 steps every day'.

'I take some comfort in that she went in her sleep and knew no pain and I'm grateful for that. I always worried about the kids driving in the car but never saw this coming. I never thought I'd ever lose a child in my life,'

Spokesperson for Melbourne's Baker Heart and Diabetes Institute said: 'there are approximately 750 cases per year of people aged under 50 in Victoria suddenly having their heart stop (cardiac arrest)' (pictured, woman suffering from chest pain)

Melbourne's Baker Heart and Diabetes Institute is developing the country's first SADS registry.

'There are approximately 750 cases per year of people aged under 50 in Victoria suddenly having their heart stop (cardiac arrest),' a spokesperson said.

'Of these, approximately 100 young people per year will have no cause found even after extensive investigations such as a full autopsy (SADS phenomenon).'

Cardiologist and researcher Dr Elizabeth Paratz said: 'Baker's registry was the first in the country and one of only a few in the world that combined ambulance, hospital and forensics information.'

'(It allows you to see) people have had the cardiac arrest and no cause was found on the back end,' Dr Paratz said.

She believes the potential lack of awareness may be due to the fact 'a lot of it takes place outside of traditional medical settings'.

Cardiologist and researcher Dr Elizabeth Paratz (pictured) said from a public health perspective, combating SADS was 'not as easy as everyone in Australia getting genetically screened' as scientists were still not 100 per cent clear on 'what genes cause this'

'The majority of these SADS events, 90 per cent, occur outside the hospital – the person doesn't make it – so it's actually ambulance staff and forensics caring for the bulk of these patients,' Dr Paratz said.

'I think even doctors underestimate it. We only see the 10 per cent who survive and make it to hospital. We only see the tip of the iceberg ourselves.'

For family and friends of victims, SADS is a 'very hard entity to grasp' because it's a 'diagnosis of nothing', Dr Paratz added.

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Dr Paratz said that from a public health perspective, combating SADS was 'not as easy as everyone in Australia getting genetically screened' as scientists were still not 100 per cent clear on 'what genes cause this'.

'The best advice would be, if you yourself have had a first-degree relative – a parent, sibling, child – who's had an unexplained death, it's extremely recommended you see a cardiologist,' she said.

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Irish Mirror: the latest news, showbiz, football and sport

Het vaccin van Johnson & Johnson . © AFP

Medicijnwaakhond VS legt coronavaccin Johnson & Johnson zware restricties op

De Amerikaanse medicijnwaakhond FDA legt het coronavaccin van Johnson & Johnson verregaande restricties op nadat het vaccin gelinkt werd aan een risico op

NET BINNEN

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MEEST GELEZEN

Boostervaccin van Sanofi en GSK

ernstige trombose (bloedstolsels). Dat heeft het FDA donderdag meegedeeld.

IB 06-05-22, 04:19 **Laatste update:** 06-05-22, 05:04 **Bron:** BELGA

Concreet mag het vaccin van Johnson & Johnson voortaan enkel nog toegediend worden aan volwassenen als een prik met Pfizer of Moderna om medische redenen of wegens stockproblemen niet mogelijk is. Daarnaast wordt ook nog een opening gemaakt voor mensen die wegens "persoonlijke twijfels" geen mRNA-vaccin wensen.
Het FDA nam de beslissing nadat het zestig gevallen van tromboses onder de loep had genomen, waarvan negen overlijdens.

Lees ook

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In de VS werden iets minder dan 19 miljoen doses van het coronavaccin van Johnson & Johnson toegediend, goed voor zowat 3 procent van het totale aantal doses.

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Studie toont hoe simpele oogtest risico op hartaanvallen kan voorspellen

PRODUKTIE 13

NEWS AND COMMENTARY

Judge Orders FDA To Expedite Release Of Pfizer Data On COVID-19 Vaccine: 'Paramount Public Importance'

By Tim Pearce

Jan 7, 2022 DailyWire.com

Jakub Porzycki/NurPhoto via Getty Images

A federal judge in Texas ordered the Food and Drug Administration (FDA) to expedite the release of hundreds of thousands of pages of documents on the Pfizer vaccine, rejecting a request by the federal government to tranche out the data over the next 75 years.

U.S. District Judge Mark Pittman of the U.S. District Court for the Northern District of Texas ruled on Thursday that the FDA must release all data submitted by Pfizer for its application for its COVID-19 vaccine's emergency use at a pace of 55,000 pages a month. The FDA had requested that it be allowed to put out the data at a far lower pace of 500 pages per month.

Pittman's ruling comes as a result of a Freedom of Information Act (FOIA) Request filed by Public Health and Medical Professionals for Transparency, a group formed to make public the data used by the FDA to grant emergency approvals for COVID-19 vaccines. Attorney Aaron Siri, who represented the group in court over the FOIA request, celebrated the ruling in a piece on Substack.

"This is a great win for transparency and removes one of the strangleholds federal 'health' authorities have had on the data needed for independent scientists to offer solutions and address serious issues with the current vaccine program – issues which include waning immunity,

variants evading vaccine immunity, and, as the CDC has confirmed, that the vaccines do not prevent transmission," Siri wrote.

"No person should ever be coerced to engage in an unwanted medical procedure," he continued. "And while it is bad enough the government violated this basic liberty right by mandating the Covid-19 vaccine, the government also wanted to hide the data by waiting to fully produce what it relied upon to license this product until almost every American alive today is dead. That form of governance is destructive to liberty and antithetical to the openness required in a democratic society."

Pittman's ruling states that the FDA must turn over 12,000 pages of documents by the end of January, then 55,000 pages every 30 days until the entirety, omitting redacted portions, of the data submitted by Pfizer has been released. The judge rejected the FDA's request for a slower release schedule citing the "paramount public importance" of the vaccine data. Pittman wrote in part:

> *Here, the Court recognizes the "unduly burdensome" challenges that this FOIA request may present to the FDA. See generally ECF Nos. 23, 30,*

> *34. But, as expressed at the scheduling conference, there may not be a "more important issue at the Food and Drug Administration . . . than the pandemic, the Pfizer vaccine, getting every American vaccinated, [and] making sure that the American public is assured that this was not [] rush[ed] on behalf of the United States . . . ." ECF No. 34 at 46. Accordingly, the Court concludes that this FOIA request is of paramount public importance.*
>
> *"[S]tale information is of little value." Payne Enters., Inc. v. United States, 837 F.2d 486, 494 (D.C. Cir. 1988). The Court, agreeing with this truism, therefore concludes that the expeditious completion of Plaintiff's request is not only practicable, but necessary. See Bloomberg, L.P. v. FDA, 500 F. Supp. 2d 371, 378 (S.D.N.Y. Aug. 15, 2007) ("[I]t is the compelling need for such public understanding that drives the urgency of the request."). To that end, the Court further concludes that the production rate, as detailed below, appropriately balances the need for unprecedented urgency in processing this request with the FDA's concerns regarding the burdens of production. See Halpern v. FBI, 181 F.3d 279, 284–85 (2nd Cir. 1991) ("[FOIA] emphasizes a preference for the fullest possible agency disclosure of such information consistent with a responsible balancing of competing concerns . . . .").*

COVID-19 Vaccine, FDA, Pfizer

Health Law & Business

Why a Judge Ordered FDA to Release Covid-19 Vaccine Data Pronto

By Aaron Siri

Jan. 18, 2022, 6:00 AM

A group of scientists and medical researchers sued the FDA under FOIA to force release of hundreds of thousands of documents related to licensing of the Pfizer-BioNTech Covid-19 vaccine. Plaintiff's attorney Aaron Siri, who is representing the group, explains the fight that led a federal court to order expedited release of documents the agency claimed it would take decades to process.

In response to a Freedom of Information Act request, the Food and Drug Administration asked a federal judge for permission to make the public wait until the year 2096 to disclose all of the data it relied upon to license Pfizer's Covid-19 vaccine.

That is not a typo. The FDA wanted court approval to have up to 75 years to publicly disclose this information.

In its attempts to build public support for Covid-19 vaccinations, the FDA repeatedly promised "full transparency," and reaffirmed its "commitment to transparency" when licensing Pfizer's Covid-19 vaccine.

With that promise in mind, after the vaccine's licensure in August 2020, Public Health and Medical Professionals for Transparency, a group of highly credentialed scientists submitted a FOIA request to the FDA for the data submitted by Pfizer. The scientists explained that, until all the data is produced, a proper review cannot be conducted because missing even a single data set could throw off any analysis.

In response, the FDA produced nothing. Therefore, in September 2021, the scientists, represented by their attorneys at Siri & Glimstad, sued the FDA demanding it produce this data by March 2022.

The agency originally estimated it would need to produce 329,000 pages, and asked the court for permission to produce just 500 pages per month, which would have taken 55 years. In its final brief to the Court, the FDA admitted that the total page count was at least 451,000, but still sought permission to produce just 500 pages per month. Meaning that it could have taken 75 years, when most Americans alive today would be dead, to fully publicly disclose this information.

On Jan. 6, a federal court in the Northern District of Texas ordered the expedited release. As of Jan. 12, the FDA hasn't indicated it intends to appeal.

Scientists Requested Data After FDA Licensing

The FDA licensed the Pfizer vaccine on Aug. 23, 2021, just 108 days after Pfizer started producing the records to the agency. During that period, the FDA asserts it conducted an intense, robust, and thorough analysis of those documents to assure the public that the Pfizer vaccine was safe and effective.

Yet, when asked to share those documents with the public, the FDA claimed it needed over 20,000 days. The FDA's production schedule clashed with its promise of transparency.

The purpose of FOIA is government transparency. When it comes to the Pfizer vaccine, the need for transparency is unprecedented. A majority of Americans are now mandated to receive a Covid-19 vaccine under penalty of losing a job, or worse.

This has never been done before. Typically adult vaccine mandates have been limited; even the seminal U.S. Supreme Court vaccine mandate decision, *Jacobson v. Massachusetts,* only involved a state-imposed $5 penalty, and school vaccine mandates have historically had liberal religious or personal belief exemption policies.

Even more problematic is that Americans, if injured, cannot sue Pfizer. There is virtually no other product where a consumer is prohibited from suing the company that manufactures, markets, and profits from the product.

Decoupling a company's profit interest from its interest in safety creates a moral hazard and departs from centuries of product liability doctrine. Thus, it is extraordinary that Americans must take this product under penalty of expulsion from work, school, the military and civil life, but they cannot sue Pfizer for any resulting injuries.

The federal government created this unprecedented situation. It granted the immunity, licensed the product, and aggressively sought mandates. This situation therefore warrants unprecedented transparency.

As then-presidential candidate Joe Biden told the American people, "You've got to make all of it [the vaccine data] available to other experts across the nation so they can look and see." He repeated that need to share the data numerous times. So did senators and representatives on both sides of the aisle.

FDA Claimed It Can't Comply, Judge Orders Compliance

The FDA apparently disagreed. During a hearing on Dec. 14, 2021, its counsel steadfastly maintained that the court should not require the agency to produce more than 500 pages per month, harping on the FDA's purported limited resources, its need to redact personal information, and duty to protect Pfizer's trade secret interests, all the while ignoring the interests of the American people.

The FDA's excuses were incredible. The FDA has more than 18,000 employees and a budget of over $6.5 billion. It would be laughable if any multibillion-dollar company came before a court and claimed poverty to escape making a document production, but that was the FDA's position.

U.S. District Judge Mark T. Pittman, Northern District of Texas, expressed dismay at the FDA's proposed rate of production. He found the duration requested by the FDA unreasonable, comparing it to the actions of totalitarian nations. As such, the judge on Jan. 6 ordered the FDA to produce at least 55,000 pages per month.

In his ruling, the judge recognized that the release of this data is of paramount public importance and should be one of the FDA's highest priorities. He quoted James Madison as saying a "popular Government, without popular information, or the means of acquiring it, is but a Prologue to a Farce or a Tragedy" and John F. Kennedy as explaining that a "nation that is afraid to let its people judge the truth and falsehood in an open market is a nation that is afraid of its people."

America has some of the greatest institutions of learning the world has ever known. We need the scientific community, both inside and outside the government, to address the serious ongoing issues with the vaccine program, including waning immunity, variants evading vaccines, and that vaccinated individuals can still transmit the virus.

The FDA's attempt to close the door and lock out independent scientists from the data necessary to address these issues was irresponsible.

Transparent, Independent Review Is Needed

The failure of the government's closed-door approach is exemplified by the fact that the FDA did not send a representative to the court hearing because, as the government attorney explained, the FDA's Covid-19 protocols would not permit it.

Meaning, despite a reported vaccination rate of over 96% across federal health agencies back in November 2021, and the FDA's claim that the vaccines are "effective," Covid-19 is still disrupting everyday life. This brings into stark focus the need to open the door and involve independent scientists.

As Pittman recognized, America needs transparency and independent scientists to review this data—not in 75 years, but now.

This article does not necessarily reflect the opinion of The Bureau of National Affairs, Inc., the publisher of Bloomberg Law and Bloomberg Tax, or its owners.

Write for Us: Author Guidelines

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PRODUKTIE 14

Moment of truth: Pfizer must prove efficacy and safety of its Covid vaccine within 48 hours in Uruguay

The judge made the order as part of a complaint to suspend childhood vaccinations in Uruguay. The extent to which the authorities and Pfizer can provide the required evidence (and whether their failure to do so will have consequences) will become clear on Wednesday.

By **Juan Martinez** - July 4, 2022

RIO DE JANEIRO, BRAZIL – Uruguay media report that a Montevideo judge has ordered disclosure of a range of information about Covid vaccines – within 48 hours. Administrative Judge Alejandro Recarey's order is directed at the government, the Ministry of Health, the state health agency, and pharmaceutical giant Pfizer.

Among other things, detailed information on the vaccine composition and evidence of its safety is required.

Read also: Check out our coverage on curated alternative narratives

Representatives of all agencies, as well as pharmaceutical giant Pfizer, are due to appear at the hearing at 9 a.m. Wednesday, where the requested information must be presented.

> EL GOBIERNO URUGUAYO Y LA FARMACÉUTICA PFIZER DISPONEN DE 48 HORAS PARA PRESENTAR ANTE LA JUSTICIA INFORMACIÓN DETALLADA DE LAS VACUNAS ANTICOVID ADMINISTRADAS EN EL PAÍS, DE ACUERDO CON UN PEDIDO JUDICIAL DIVULGADO EN LAS ÚLTIMAS HORAS.HTTPS://T.CO/OTDDEKPGPY
>
> — TELENOCHE (@TELENOCHEUY) JULY 4, 2022

The judge made the order as part of a complaint to suspend childhood vaccinations in Uruguay.

According to the decree, the following information is requested:

- The vaccine purchase contracts between the Uruguayan government and Pfizer, as well as information on whether clauses for civil compensation or immunity from punishment for suppliers in the event of possible side effects, are included
- Information on the distribution of the vaccine batches, as well as quality control measures
- Detailed information on the biochemical composition of the vaccine – including whether graphene oxide and nanotechnology components are included
- Information on the mRNA used and evidence that it is harmless
- A statement whether the vaccine or parts of its ingredients are experimental
- Detailed data demonstrating the efficacy and safety of the vaccination, i.e., "the negative or positive impact of the so-called vaccination on the number of infections and deaths diagnosed with Covid from the beginning of the campaign to the present"
- Detailed information on the average age of those who died with Covid-19 diagnosis and information on how many of those deaths were caused solely by the disease
- Information on whether studies are being conducted on the increase in deaths in Uruguay since the vaccination campaign began in March 2021
- Scientific evidence that unvaccinated people pose a risk
- Information on those responsible for and involved in the vaccination campaign and their links to NGOs or (pharmaceutical) companies
- Information on the extent to which alternative therapies against covid-19 have been investigated

> FALLO HISTORICO EN URUGUAY, UN VERDADERO "MARACANAZO JUDICIAL";JUEZ ORDENA AL GOBIERNO MOSTRAR CONTRATO DE LAS VACUNAS Y MÚLTIPLES MEDIDAS INVESTIGATIVAS, COMO POR EJEMPLO, DECLARACIÓN DE AUTORIDADES DE PFIZER. VIDEO EXPLICATIVO DEL FALLO DEL JUEZ RECAREY HTTPS://T.CO/35TSE599CP
>
> — DR. SALLE LORIER (@SALLELORIER) JULY 2, 2022

The extent to which the authorities and Pfizer can provide the required evidence (and whether their failure to do so will have consequences) will become clear on Wednesday.

Juan Martinez

Juan Martinez is a Chilean economist and journalist. He lives in South Florida and specializes in reporting on Latin America.

Pfizer Withdraws from Uruguay After Government Demands Company Disclose Contents of Vaccine

Posted on July 7, 2022 by Constitutional Nobody

Tales from the Conspiratum

Uruguayan judge demands explanations regarding Pfizer's COVID-19 vax

An Uruguayan court has ruled that the national government and the laboratory Pfizer must disclose during a hearing this coming Wednesday the exact components of the COVID-19 vaccine of that brand which is widely used throughout the country.

The Uruguayan government and the pharmaceutical were given 48 hours by Judge Alejandro Recarey to submit detailed information on the anticovid vaccines while dealing with an injunction request to halt vaccination among children aged 5 and over which is nevertheless carried out voluntarily.

As per the court's decision, the Executive and the U.S. laboratory will have to provide documentation on the composition of the vaccines, including the possible presence of "graphene oxide" or "nanotechnological elements," it was reported.

Also requested are data demonstrating the "innocuousness" of "the substance called messenger RNA" and that "the experimental nature" of the vaccines be accredited.

The judge also demanded explanations as to whether studies have been carried out "to explain the notorious increase in deaths due to covid-19 as of March 2021 in relation to the previous year."

Pfizer will also have to address the issue "of adverse effects of the vaccines against the so-called Covid-19. In general, and also in detail in relation to the child population," according to the court document.

Representatives of the Uruguayan Presidency and the Health Ministry as well as from the US pharmaceutical company are to appear at Wednesday's hearing.

The Uruguayan Ministry of Public Health, the State Health Services Administration, and the Presidency have also been required to submit all the information regarding the contract for the purchase of vaccines, where the clauses of civil indemnity or criminal impunity of the suppliers in the event of adverse effects are to be examined.

PRODUKTIE 15

INDIA

FEBRUARY 5, 2021 / 2:30 AM / UPDATED A YEAR AGO

Pfizer drops India vaccine application after regulator seeks local trial

By Krishna N. Das

NEW DELHI (Reuters) - Pfizer Inc said on Friday it had withdrawn an application for emergency-use authorisation of its COVID-19 vaccine in India, after failing to meet the drug regulator's demand for a local safety and immunogenicity study.

A vial and sryinge are seen in front of a displayed Pfizer and Biontech logo in this illustration taken January 11, 2021. REUTERS/Dado Ruvic/Illustration/File Photo

Unlike other companies conducting small studies in India for foreign-developed vaccines, Pfizer had sought an exception citing approvals it had received elsewhere based on trials done in countries such as the United States and Germany.

Indian health officials say they generally ask for so-called bridging trials to determine if a vaccine is safe and generates an immune response in its citizens. There are, however, provisions under India's rules to waive such trials in certain conditions.

The U.S. company, which was the first drugmaker to seek emergency approval in India for its vaccine developed with Germany's BioNTech, made the withdrawal decision after a meeting with India's Central Drugs Standard Control Organisation (CDSCO) on Wednesday.

The drug regulator said on its website its experts did not recommend the vaccine because of side effects reported abroad were still being investigated. It also said Pfizer had not proposed any plan to generate safety and immunogenicity data in India.

"Based on the deliberations at the meeting and our understanding of additional information that the regulator may need, the company has decided to withdraw its application at this time," Pfizer said in a statement.

"Pfizer will continue to engage with the authority and re-submit its approval request with additional information as it becomes available in the near future."

Reuters was the first to break the news.

Pfizer had sought authorisation for its vaccine in India late last year, but the government in January approved two much cheaper shots - one from Oxford University/AstraZeneca and another developed in India by Bharat Biotech with the Indian Council of Medical Research.

PRODUKTIE 16

Food and Chemical Toxicology 164 (2022) 113008

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Food and Chemical Toxicology

journal homepage: www.elsevier.com/locate/foodchemtox

Innate immune suppression by SARS-CoV-2 mRNA vaccinations: The role of G-quadruplexes, exosomes, and MicroRNAs

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Cancer

ABSTRACT

The mRNA SARS-CoV-2 vaccines were brought to market in response to the public health crises of Covid-19. The utilization of mRNA vaccines in the context of infectious disease has no precedent. The many alterations in the vaccine mRNA hide the mRNA from cellular defenses and promote a longer biological half-life and high production of spike protein. However, the immune response to the vaccine is very different from that to a SARS-CoV-2 infection. In this paper, we present evidence that vaccination induces a profound impairment in type I interferon signaling, which has diverse adverse consequences to human health. Immune cells that have taken up the vaccine nanoparticles release into circulation large numbers of exosomes containing spike protein along with critical microRNAs that induce a signaling response in recipient cells at distant sites. We also identify potential profound disturbances in regulatory control of protein synthesis and cancer surveillance. These disturbances potentially have a causal link to neurodegenerative disease, myocarditis, immune thrombocytopenia, Bell's palsy, liver disease, impaired adaptive immunity, impaired DNA damage response and tumorigenesis. We show evidence from the VAERS database supporting our hypothesis. We believe a comprehensive risk/benefit assessment of the mRNA vaccines questions them as positive contributors to public health.

1. Introduction

Vaccination is an endeavor to utilize non-pathogenic material to mimic the immunological response of a natural infection, thereby conferring immunity in the event of pathogen exposure. This goal has been primarily pursued through the use of both whole organism and attenuated virus vaccines. Use of fragments of virus or their protein products, referred to as "subunit vaccines," has been more technically challenging (Bhurani et al., 2018). In any event, an implicit assumption behind the deployment of any vaccination campaign is that the vaccine confers the effects of a 'benign infection,' activating the immune system against future exposure, while avoiding the health impacts of actual infection.

Much of the literature on this related to COVID-19 suggests that the immune response to mRNA-based vaccination is similar to natural infection. A preprint study found "high immunogenicity of BNT162b2 vaccine in comparison with natural infection." The authors found there to be many qualitative similarities though quantitative differences (Psichogiou et al., 2021a). Jhaveri (2021) suggests that mRNA vaccines do what infection with the virus does: "The protein is produced and presented in the same way as natural infection." The U.S. Centers for Disease Control and Prevention (CDC) makes the case based upon antibody titers generated by prior infection vs. vaccination, in addition to production of memory B cells, to argue that the immune response to vaccination is analogous to the response to natural infection (Centers for Disease Control and Prevention, 2021a). It is this similarity in the humoral immune response to vaccination vs natural infection, paired with both trial and observational data demonstrating reduced risk of infection following vaccination, that stands as the justification for the mass vaccination campaign.

Our paper summarizes the current literature on mRNA and its effects on the molecular biology within human cells. We recognize that there is a wide range of opinions in this nascent phase of mRNA technology. Given its widespread deployment ahead of basic work on so many of the

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Available online 15 April 2022

mechanisms we discuss here, we believe that our work is important for providing a broad understanding of present and future reviews that relate to the burgeoning preclinical molecular work being done in this area.

In this paper, we explore the scientific literature suggesting that vaccination with an mRNA vaccine initiates a set of biological events that are not only different from that induced by infection but are in several ways demonstrably counterproductive to both short- and long-term immune competence and normal cellular function. These vaccinations have now been shown to downregulate critical pathways related to cancer surveillance, infection control, and cellular homeostasis. They introduce into the body highly modified genetic material. A preprint has revealed a remarkable difference between the characteristics of the immune response to an infection with SARS-CoV-2 as compared with the immune response to an mRNA vaccine against COVID-19 (Ivanova et al., 2021). Differential gene expression analysis of peripheral dendritic cells revealed a dramatic upregulation of both type I and type II interferons (IFNs) in COVID-19 patients, but not in vaccinees. One remarkable observation they made was that there was an expansion of circulating hematopoietic stem and progenitor cells (HSPCs) in COVID-19 patients, but this expansion was notably absent following vaccination. A striking expansion in circulating plasmablasts observed in COVID-19 patients was also not seen in the vaccinees. All of these observations are consistent with the idea that the anti-COVID-19 vaccines actively suppress type I IFN signaling, as we will discuss below. In this paper we will be focusing extensively, though not exclusively, on vaccination-induced type I IFN suppression and the myriad downstream effects this has on the related signaling cascade.

Since long-term pre-clinical and Phase I safety trials were combined with Phase II trials, then phase II and III trials were combined (Kwok, 2021); and since even those were terminated early and placebo arms given the injections, we look to the pharmacosurveillance system and published reports for safety signals. In doing so, we find that that evidence is not encouraging. The biological response to mRNA vaccination as it is currently employed is demonstrably *not* similar to natural infection. In this paper we will illustrate those differences, and we will describe the immunological and pathological processes we expect are being initiated by mRNA vaccination. We will connect these underlying physiological effects with both realized and yet-to-be-observed morbidities. We anticipate that implementation of booster vaccinations on a wide scale will amplify all of these problems.

The mRNA vaccines manufactured by Pfizer/BioNTech and Moderna have been viewed as an essential aspect of our efforts to control the spread of COVID-19. Countries around the globe have been aggressively promoting massive vaccination programs with the hope that such efforts might finally curtail the ongoing pandemic and restore normalcy. Governments are reticent to consider the possibility that these injections might cause harm in unexpected ways, and especially that such harm might even surpass the benefits achieved in protection from severe disease. It is now clear that the antibodies induced by the vaccines fade in as little as 3–10 weeks after the second dose (Shrotri et al., 2021), such that people are being advised to seek booster shots at regular intervals (Centers for Disease Control and Prevention, 2021b). It has also become apparent that rapidly emerging variants such as the Delta and now the Omicron strain are showing resistance to the antibodies induced by the vaccines, through mutations in the spike protein (Yahi et al., 2021). Furthermore, it has become clear that the vaccines do not prevent transmission of the disease, but can only be claimed to reduce symptom severity (Kampf, 2021a). A study comparing vaccination rates with COVID-19 infection rates across 68 countries and 2947 counties in the United States in early September 2021, found no correlation between the two, suggesting that these vaccines do not protect from spread of the disease (Subramanian and Kumar, 2947). Regarding symptom severity, even this aspect is beginning to be in doubt, as demonstrated by an outbreak in an Israeli hospital that led to the death of five fully vaccinated hospital patients (Shitrit et al., 2021). Similarly, Brosh-Nissimov et al. (2021) reported that 34/152 (22%) of fully vaccinated patients among 17 Israeli hospitals died of COVID-19.

The increasing evidence that the vaccines do little to control disease spread and that their effectiveness wanes over time make it even more imperative to assess the degree to which the vaccines might cause harm. That SARS-CoV-2 modified spike protein mRNA vaccinations have biological impacts is without question. Here we attempt to distinguish those impacts from natural infection, and establish a mechanistic framework linking those unique biological impacts to pathologies now associated with vaccination. We recognize that the causal links between biological effects initiated by mRNA vaccination and adverse outcomes have not been established in the large majority of cases.

2. Interferons: an overview with attention to cancer surveillance

Discovered in 1957, interferon (IFN) earned its name with the recognition that cells challenged by attenuated influenza A virus created a substance that "interfered with" a subsequent infection by a live virus (Lindenmann, 1982). IFN is now understood to represent a very large family of immune-modulating proteins, divided into three types, designated as type I, II, and III based upon the receptors each IFN interacts with. Type I IFN includes both IFN-α and IFN-β, and this type is the most diverse, being further divided into seventeen subtypes. IFN-α alone has thirteen subtypes currently identified, and each of those is further divided into multiple categories (Wang et al., 2017a). Type I IFNs play a powerful role in the immune response to multiple stressors. In fact, they have enjoyed clinical therapeutic value as a treatment option for a variety of diseases and conditions, including viral infections, solid tumors, myeloproliferative disorders, hematopoietic neoplasms and autoimmune diseases such as multiple sclerosis (Passegu and Ernst, 2009).

As a group, IFNs play exceedingly complicated and pleiotropic roles that are coordinated and regulated through the activity of the family of IFN regulatory factors, or IRFs (Kaur and Fang, 2020). IRF9 is most directly involved in anti-viral as well as anti-tumor immunity and genetic regulation (Alsamman and El-Masry, 2018; Huang et al., 2019; Zitvogel et al., 2015).

Closely related to this are plasmacytoid dendritic cells (pDCs), a rare type of immune cell that circulate in the blood but migrate to peripheral lymphoid organs during a viral infection. They respond to a viral infection by sharply upregulating production of type I IFNs. The IFN-α released in the lymph nodes induces B cells to differentiate into plasmablasts. Subsequently, interleukin-6 (Il-6) induces plasmablasts to evolve into antibody-secreting plasma cells (Jego et al., 2003). Thus, IFNs play a critical role in both controlling viral proliferation and inducing antibody production. Central to both antiviral and anticancer immunity, IFN-α is produced by macrophages and lymphocytes when either is challenged with viral or bacterial infection or encounters tumor cells (De Andrea et al., 2002). Its role as a potent antiviral therapy has been recognized in the treatment of hepatitis C virus complications (Feng et al., 2012), Cytomegalovirus infection (Delannoy et al., 1999), chronic active ebola virus infection (Sakai et al., 1998), inflammatory bowel disease associated with herpes virus infection (Ruther et al., 1998), and others.

Impaired type I IFN signaling is linked to many disease risks, most notably cancer, as type I IFN signaling suppresses proliferation of both viruses and cancer cells by arresting the cell cycle, in part through upregulation of p53, a tumor suppressor gene, and various cyclin-dependent kinase inhibitors (Musella et al., 2017; Matsuoka et al., 1998). IFN-α also induces major histocompatibility (MHC) class 1 antigen presentation by tumor cells, causing them to be more readily recognized by the cancer surveillance system (Heise et al., 2016; Sundstedt et al., 2008). The range of anticancer effects initiated by IFN-α expression is astounding and occurs through both direct and indirect mechanisms. Direct effects include cell cycle arrest, induction of cell

differentiation, initiation of apoptosis, activation of natural killer and $CD8^+$ T cells, and others (Schneider et al., 2014).

The indirect anticancer effects are predominantly carried out through gene transcription activation of the Janus kinase signal transducer and activator of transcription (JAK/STAT) pathway. IFN-α binding on the cell surface initiates JAK, a tyrosine kinase, to phosphorylate STAT1 and STAT2 (Asmana Ningrum, 2014). Once phosphorylated, these STATs form a complex with IRF9, one of a family of IRFs that play a wide range of roles in oncogene regulation and other cell functions (Takaoka et al., 2008). It is this complex, named IFN-stimulated gene factor 3 (ISGF3), that translocates to the cell nucleus to enhance the expression of at least 150 genes (Schneider et al., 2014). IRF9 has been suggested to be the primary member of the IRF family of proteins responsible for activation of the IFN-α antiproliferative effects, and that appears to be through its binding to the tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) receptor 1 and 2 (TRAIL-R1/2) (Tsuno et al., 2009). IRF7 is another crucial member of the IRF family of proteins involved early in the response to a viral infection. It is normally expressed in low amounts but is strongly induced by ISGF3. IRF7 also undergoes serine phosphorylation and nuclear translocation to further activate the immune response. IRF7 has a very short half-life, so its gene-induction process is transient, perhaps to avoid overexpression of IFNs (Honda et al., 2006).

Once TRAIL is bound by IRF9, it is then able to act as a ligand for Death Receptor 4 (DR4) or DR5, initiating a cascade of events involving production of caspase 8 and caspase 3, and ultimately triggering apoptosis (Sayers, 2011). Dysregulation of this pathway, through suppression of either IFN-α or IRF9 and the resulting failure to bind TRAIL-R, has been associated with several hematologic malignancies (Testa, 2010) and has been shown to increase the metastatic potential in animal models of melanoma, colorectal cancer, and lymphoma (Finnberg and El-Deiry, 2008).

IFN-α both initiates and orchestrates a wide range of cancer suppressing roles. Dunn et al. (2005) showed that IFN-α plays an active role in cancer immunoediting, its locus of action being hematopoietic cells that are "programmed" via IFN-α binding for tumor surveillance. It is via the exceedingly complex interactions between type I IFNs and IRF7 and IRF9 in particular that a great deal of antiproliferative effects are carried out. This is evidenced by the large number of studies showing increased tumor growth and/or metastases associated with a wide number of cancer types.

For example, Bidwell et al. (2012) found that, among over 800 breast cancer patients, those with high expression of IRF7-regulated genes had significantly fewer bone metastases, and they propose assessment of these IRF7-related gene signatures as a way to predict those at greatest risk. Use of microRNA to target IRF7 expression has also been shown to enhance breast cancer cell proliferation and invasion *in vitro* (Li et al., 2015). Zhao et al. (2017) found a similar role for IRF7 in relation to bone metastases in a mouse model of prostate cancer. Regarding the anti-cancer mechanism behind IRF7 expression, Solis et al. (2006) found that IRF7 induces transcription of multiple genes and translation of their downstream protein products including TRAIL, IL-15, ISG-56 and CD80, with the noted therapeutic implications.

IRF9, too, has a central role to play in cancer surveillance and prevention. Erb et al. (2013) demonstrated that IRF9 is the mediator through which IL-6 augments the anti-proliferation effects of IFN-α against prostate cancer cells. Tian et al. (2018) found IRF9 to be a key negative regulator of acute myeloid leukaemia cell proliferation and evasion of apoptosis. It does so, at least in part, through acetylation of the master regulatory protein p53.

Both IFN-α and IRF9 are also apparently necessary for the cancer-preventative properties of a fully functional BRCA2 gene. In a study presented as an abstract at the First AACR International Conference on Frontiers in Basic Cancer Research, Mittal and Chaudhuri (2009) describe a set of experiments which show for the first time that BRCA2 expression leads to increased IFN-α production and augments the signal transduction pathway resulting in the complexing of IRF9, STAT1 and STAT2 described previously. Two years prior, Buckley et al. (2007) had established that BRCA1 in combination with IFN-γ promotes type I IFNs and subsequent production of IRF7, STAT1, and STAT2. Thus, the exceedingly important cancer regulatory genes BRCA1 and BRCA2 rely on IRF7 and IRF9, respectively, to carry out their protective effects. Rasmussen et al. (2021) reviewed compelling evidence that deficiencies of either IRF7 or IRF9 lead to significantly greater risk of severe COVID-19 illness. Importantly, they also note that evidence suggests type I IFNs play a singularly important role in protective immunity against COVID-19 illness, a role that is shared by multiple cytokines in most other viral illnesses including influenza.

As will be discussed in more detail below, the SARS-CoV-2 spike glycoprotein modifies host cell exosome production. Transfection of cells with the spike protein's gene and subsequent SARS-CoV-2 spike protein production results in those cells generating exosomes containing microRNAs that suppress IRF9 production while activating a range of pro-inflammatory gene transcripts (Mishra and Banerjea, 2021). Since these vaccines are specifically designed to induce high and ongoing production of SARS-CoV-2 spike glycoproteins, the implications are ominous. As described above, inhibition of IRF9 will suppress TRAIL and all its regulatory and downstream apoptosis-inducing effects. IRF9 suppression via exosomal microRNA should also be expected to impair the cancer-protective effects of BRCA2 gene activity, which depends on that molecule for its activity as described above. BRCA2-associated cancers include breast, fallopian tube, and ovarian cancer for women, prostate and breast cancer for men, acute myeloid leukaemia in children, and others (National Cancer Institute, 2021).

Vaccination has also been demonstrated to suppress both IRF7 and STAT2 (Liu et al., 2021). This can be expected to interfere with the cancer-protective effects of BRCA1 as described above. Cancers associated with impaired BRCA1 activity include breast, uterine, and ovarian cancer in women; prostate and breast cancer in men; and a modest increase in pancreatic cancer for both men and women (Cancer risk and BRCA1 gene, 2021).

Reduced BRCA1 expression is linked to both cancer and neurodegeneration. BRCA1 is a well-known breast cancer susceptibility gene. BRCA1 inhibits breast cancer cell proliferation through activation of SIRT1 and subsequent suppression of the androgen receptor (Zhang et al., 2016). In a study conducted by Suberbielle et al. (2015), reduced levels of BRCA1 were found in the brains of Alzheimer's patients. Furthermore, experiments with knocking down neuronal BRCA1 in the dentate gyrus of mice showed that DNA double-strand breaks were increased, along with neuronal shrinkage and impairments in synaptic plasticity, learning and memory.

Analysis detailed in a recent case study on a patient diagnosed with a rare form of lymphoma called angioimmunoblastic T cell lymphoma provided strong evidence for unexpected rapid progression of lymphomatous lesions after administration of the BNT162b2 mRNA booster shot (Goldman et al., 2021). Comparisons of detailed metrics for hypermetabolic lesions conducted immediately before and 21 days after the vaccine booster revealed a five-fold increase after the vaccine, with the post-booster test revealing a 2-fold higher activity level in the right armpit compared to the left one. The vaccine had been injected on the right side. It is worth pointing out in this regard that lymphoid malignancies have been associated with suppression of TRAIL-R1 (MacFarlane et al., 2005).

Given the universally recognized importance of optimally functioning BRCA1/2 for cancer prevention and given the central role of the TRAIL signal transduction pathway for additional cancer surveillance, the suppression of IRF7 and IRF9 through vaccination and subsequent SARS-CoV-2 spike glycoprotein production is extremely concerning for long-term cancer control in SARS-CoV-2 mRNA genetic vaccine injected populations.

3. Considerations in the design of mRNA vaccines

Over the last three decades, the mRNA technological platform aimed to develop effective and safe nucleic acid therapeutic tools is said to have overcome serious obstacles on the coded product instability, the overwhelming innate immunogenicity, and on the delivery methodologies (Pardi et al., 2018). One of the major success stories of mRNA use as a genetic vaccination tool is on the introduction of robust immunity against cancer (Van Lint et al., 2015). In addition, the potential of mRNAs to restore or replace various types of proteins in cases of rare genetic metabolic disorders like Fabry disease has offered great potential therapeutic alternatives where no other medication has proved to be successful (Martini and Guey, 2019). However, in the case of mRNA use as genetic vaccines against infectious diseases, the preliminary safety investigations seemed to be premature for a world-wide use in the general population (Pardi et al., 2018; Doulberis et al., 2021).

Although there are essential epitopes on other SARS-CoV-2 proteins where an antibody response could have provided essential immunogenicity, well known from SARS-CoV-1 (Gordon et al., 2020), the primary goal of the developers of the SARS-CoV-2 mRNA vaccines was to design a vaccine that could induce a robust antibody response exclusively to the spike glycoprotein. Such antibodies, especially IgA in the nasopharynx, should cause the invading viruses to be quickly cleared before they could invade host cells, thus arresting the disease process early on. As stated succinctly by Kaczmarek et al. (2021):

"The rationale behind vaccination is to provide every vaccinated person with protection against the SARS-CoV-2 virus. This protection is achieved by stimulating the immune system to produce antibodies against the virus and to develop lymphocytes that will retain memory and the ability to fight off the virus for a long time." However, since vaccination is given parenterally, IgG is the principal antibody class that is raised against the SARS-CoV-2 spike glycoprotein, not IgA (Wisnewski et al., 2021).

Vaccines generally depend upon adjuvants such as aluminum and squalene to provoke immune cells to migrate to the injection site immediately after vaccination. In the history of mRNA vaccine development, it was initially hoped that the mRNA itself could serve as its own adjuvant. This is because human cells recognize viral RNA as foreign, and this leads to upregulation of type I IFNs, mediated via toll like receptors such as TLR3, TLR7 and TLR8 (Karik ó et al., 2005).

However, with time it became clear that there were problems with this approach, both because the intense reaction could cause flu-like symptoms and because IFN-α could launch a cascade response that would lead to the breakdown of the mRNA before it could produce adequate amounts of SARS-CoV-2 spike glycoprotein to induce an immune response (de Beuckelaer et al., 2016). A breakthrough came when it was discovered experimentally that the mRNA coding for the spike protein could be modified in specific ways that would essentially fool the human cells into recognizing it as harmless human RNA. A seminal paper by Karikó et al. (2005) demonstrated through a series of *in vitro* experiments that a simple modification to the mRNA such that all uridines were replaced with pseudouridine could dramatically reduce innate immune activation against exogenous mRNA. Andries et al. (2015) later discovered that 1-methylpseudouridine as a replacement for uridine was even more effective than pseudouridine and could essentially abolish the TLR response to the mRNA, preventing the activation of blood-derived dendritic cells. This modification is applied in both the mRNA vaccines on the market (Park et al., 2021).

Rather prophetically, the extensive review by Forni and Mantovani (2021) has raised serious questions about the development of innate immunity by the mRNA SARS-CoV-2 genetic vaccinations. As the authors declared: "Due to the short development time and the novelty of the technologies adopted, these vaccines will be deployed with several unresolved issues that only the passage of time will permit to clarify." Subsequently, the authors recommended including certain molecules such as the long pentraxin PTX3 as representative humoral immunity markers to assess the early activation of innate immune mechanisms and the underlying reactogenicity under the BIOVACSAFE consortium protocols (Forni and Mantovani, 2021; Weiner et al., 2019). However, to the best of our knowledge these safety protocols have not been included in the assessment of induced innate immunity by the SARS-CoV-2 mRNA genetic vaccines (Mulligan et al., 2020).

In this regard, in the case of SARS-CoV-2 BNT162b2 mRNA vaccine, unlike the immune response induced by natural SARS-CoV-2 infection, where a robust interferon response is observed, those vaccinated with BNT162b2 mRNA vaccines developed a robust adaptive immune response which was restricted only to memory cells, i.e., an alternative route of immune response that bypassed the IFN mediated pathways (Mulligan et al., 2020). Furthermore, due to subsequent mutations in the SARS-CoV-2 spike protein, there is a substantial loss of neutralizing antibodies induced by the BNT162b2 mRNA vaccine compared to those conferred by the SARS-CoV-2 mutants alone (Collier et al., 2021). In that respect, as vaccine developers admit: "Vaccine RNA can be modified by incorporating 1-methylpseudouridine, which dampens innate immune sensing and increases mRNA translation *in vivo*." (Mulligan et al., 2020; Katalin Karikó et al., 2008). Bearing in mind the multiple mutations that SARS-CoV-2 develops, as for example in the Brazil outbreaks (Timmers et al., 2021), an effective immune response that prevents the spread of SARS-CoV2 mutants necessarily involves the development of a robust IFN-I response as a part of the innate immune system. This response also requires the involvement of a functional NF-κB response. Unfortunately, spike glycoprotein overexpression dismantles the NF-κB pathway responses, and this molecular event can be augmented by spike-protein-coding mRNAs (Kyriakopoulos and McCullough, 2021; Jiang and Mei, 2021).

For successful mRNA vaccine design, the mRNA needs to be encapsulated in carefully constructed particles that can protect the RNA from degradation by RNA depolymerases. The mRNA vaccines are formulated as lipid nanoparticles containing cholesterol and phospholipids, with the modified mRNA complexed with a highly modified polyethylene glycol (PEG) lipid backbone to promote its early release from the endosome and to further protect it from degradation (Hou et al., 2021). The host cell's existing biological machinery is co-opted to facilitate the natural production of protein from the mRNA through endosomal uptake of a lipid particle (Hou et al., 2021). A synthetic cationic lipid is added as well, since it has been shown experimentally to work as an adjuvant to draw immune cells to the injection site and to facilitate endosomal escape. de Beuckelaer et al. (2016) observed that "condensing mRNA into cationic lipoplexes increases the potency of the mRNA vaccine evoked T cell response by several orders of magnitude." Another important modification is that they replaced the code for two adjacent amino acids in the genome with codes for proline, which causes the spike glycoprotein to stay in a prefusion stabilized form (Wrapp et al., 2020).

The SARS-CoV-2 spike glycoprotein mRNA is further "humanized" with the addition of a guanine-methylated cap, 3′ and 5′ untranslated regions (UTRs) copied from those of human proteins, and finally a long poly(A) tail to further stabilize the RNA (Kyriakopoulos and McCullough, 2021). In particular, researchers have cleverly selected the 3′UTR taken from globins which are produced in large quantities by erythrocytes, because it is very effective at protecting the mRNA from degradation and maintaining sustained protein production (Orlandini von Niessen et al., 2019). This is to be expected, since erythrocytes have no nucleus, so they are unable to replace the mRNAs once they are destroyed. Both the Moderna and the Pfizer vaccines adopted a 3′UTR from globins, and the Pfizer vaccine also uses a slightly modified globin 5′UTR (Xia, 2021). de Beuckelaer et al. (2016) aptly summed up the consequences of such modifications as follows: "Over the past years, technical improvements in the way IVT *[in vitro* transcribed] mRNAs are prepared (5′ Cap modifications, optimized GC content, improved polyA tails, stabilizing UTRs) have increased the stability of IVT mRNAs to such extent protein expression can now be achieved for days after direct

in vivo administration of the mRNA."

However, the optimized analogue cap formation of synthetic mRNAs inevitably forces the recipient cells to undergo a cap-dependent prolonged translation, ignoring homeostatic demands of cellular physiology (Kyriakopoulos and McCullough, 2021). The cap 2'-O methylation carried out by cap 2′-O methyltransferase (CMTR1) serves as a motif that marks the mRNA as "self," to prevent recognition by IFN-induced RNA binding proteins (Williams et al., 2020). Thus, the mRNA in the vaccines, equipped with the cap 2'-O methylation motif, evades detection as a viral invasion. Furthermore, the overwhelming impetus for cells to perform a single and artificial approach to translation according to the robust capping and synthetic methylations of mRNAs in vaccines is fundamentally associated with disease progression due to differential rather than normal signaling of pattern recognition receptors (PRRs) (Leung and Amarasinghe, 2016).

The regulatory process controlling mRNA translation is extremely complex, and it is highly disturbed in the context of mRNA vaccines (Kyriakopoulos and McCullough, 2021; Leung and Amarasinghe, 2016). Briefly, the idea is for mRNA vaccines to achieve the intended goal (i.e., production of the modified spike protein) through a stealth strategy that bypasses the natural immunological response to RNA-type viral infection. Injected lipid nanoparticles containing mRNA are brought to the cell interior via endocytosis. The mRNA escapes its lipid carrier and migrates to the ribosome, where it is abundantly translated into its final protein product, following an optimized program for producing large quantities of a specific protein over an extended period of time. These modified SARS-CoV-2 spike glycoproteins then follow one of three primary pathways. Some are proteolytically degraded and fragments are bound by MHC class I molecules for surface presentation to cytotoxic T-cells. A second pathway has those same spike glycoprotein fragments bind MHC class II molecules, move to the cell surface, and activate T-helper cells. A final pathway has soluble spike glycoproteins extruded from the cell in exosomes, where they can be recognized by B-cell-activated spike-glycoprotein-specific antibodies (Chaudhary et al., 2021).

A recent early-release study has found that the mRNA in the COVID-19 vaccines is present in germinal centers in secondary lymphoid tissue long after the vaccine is administered, and that it continues to synthesize spike glycoprotein up to at least sixty days post-vaccination (Röltgen et al., 2022). This suggests that immune cells taking up the mRNA in the arm muscle migrate into the lymph system to the lymph nodes, presumably in order to expose B-cells and T-cells to the toxic antigen. The persistence of the mRNA in the lymph nodes and its sustained synthesis of SARS-CoV-2 spike glycoprotein reflect the clever engineering involved in the mRNA technology, as described above.

In the end, it is through utilization of nanolipids and sophisticated mRNA technology that the normal immune response to exogenous RNA is evaded in order to produce a strong antibody response against an exogenous RNA virus.

4. GC enrichment and potential G4 (pG4) structures in vaccine mRNAs

Recently, members of our team investigated possible alterations in secondary structure of mRNAs in SARS-CoV-2 vaccines due to codon optimization of synthetic mRNA transcripts (McKernan et al., 2021). This study has shown that there is a significant enrichment of GC content in mRNAs in vaccines (53% in BNT162b2 and 61% in Moderna mRNA-1273) as compared to the native SARS-CoV-2 mRNA (36%). The enriched GC content of mRNAs is the result of codon optimization performed during the development of the mRNAs used in SARS-CoV-2 vaccines, apparently without determining the effect on secondary structures, particularly the Guanine quadruplex (G quadruplex) formation (McKernan et al., 2021).

Codon optimization describes the production of synthetic, codon-optimized polypeptides and proteins used in biotechnology therapeutics (such as the synthetic mRNAs used for SARS-CoV-2 vaccination). The altered codon assignments within the mRNA template dramatically increase the quantity of polypeptides and/or proteins produced (Mauro and Chappell, 2014). Synonymous codon replacement also results in a change in the multifunctional regulatory and structural roles of resulting proteins (Shabalina et al., 2013). For this reason, codon optimization has been cautioned against due to its consequent changes causing perturbation in the secondary conformation of protein products with potentially devastating effects on their resulting immunogenicity, efficacy and function (Zhou et al., 2013; Agashe et al., 2013). Notably, various human diseases are the result of synonymous nucleotide polymorphisms (McCarthy et al., 2017).

In an experiment where GC-rich and GC-poor versions of mRNA transcripts for heat shock protein 70 were configured in the context of identical promoters and UTR sequences, it was found that GC-rich genes were expressed several-fold to over a hundred-fold more efficiently than their GC-poor counterparts (Kudla et al., 2006). This is partly because all of the preferred mammalian codons have G or C nucleotides in the third position. It is also well documented that AU-rich elements in the 3' UTRs can destabilize mRNA (Otsuka et al., 2019). What may be of particular concern is the fact that GC enrichment content in vaccine mRNAs results in an enhanced ability for potential G-quadruplex (pG4) formations in these structures, and this could cause onset of neurological disease (Wang et al., 2021). Remarkably, the human prion protein (PrP) genetic sequence contains multiple G4 forming motifs, and their presence may form the missing link in the initial conversion of PrP to the misfolded form, PrPsc (Olsthoorn, 2014). PrP binding to its own mRNA may be the seed that causes the protein to misfold. This observation is particularly concerning in light of the fact that the SARS-CoV-2 spike glycoprotein has prion-like characteristics (Tetz and Tetz, 2022).

On the one hand, the GC content has a key role in the modulation of translation efficiency and control of mRNA expression in mammals (Babendure et al., 2006). Especially during translation initiation, the GC content operating as a cis-acting mRNA element orchestrates the 43S ribosomal pre-initiation complex attachment and thereafter the assembly of the eukaryotic translation initiation factor 4F (eIF4F) complex. One representative example of this system in action is the regulation of α and β globin mRNA expression through their 5′ untranslated regions (5′UTRs) (Babendure et al., 2006).

On the other hand, the presence of pG4s in RNAs is implicated in cancer biology as key determinants of the regulation of G4 RNA binding proteins such as helicase (Herdy et al., 2018). Generally, the G-quadruplexes in RNAs have essential roles in a) the regulation of gene expression, b) the localization of ribonuclear proteins, c) the mRNA localization and d) the regulation of proto-oncogene expression (Fay et al., 2017).

Regarding SARS-CoV-2, relevant studies reveal overwhelming similarities between SARS-CoV-2 pG4s, including in RNA coding for SARS-CoV-2 spike glycoprotein, and those sequenced in the human transcriptome (Zhang et al., 2020). Thus, it can be inferred that synthetic mRNAs in vaccines carrying more pG4 structures in their coding sequence for SARS-CoV-2 spike glycoprotein will amplify and compound the potential post-transcriptional disorganization due to G4-enriched RNA during natural SARS-CoV-2 infection. Moreover, the cellular nucleic acid binding protein (CNBP), which is the main cellular protein that binds to the SARS-CoV-2 RNA genome in human-infected cells (Schmidt et al., 2021), binds to and promotes the unfolding of SARS-CoV-2 G4s formed by both positive and negative sense template strands of the SARS-CoV-2 RNA genome. A similar modulation of CNBP on vaccine mRNA G4s and promotion of G4 equilibrium towards unfolded conformations create favorable conditions for miRNA binding, and this will have a direct impact on miRNA-dependent regulation of gene expression (Rouleau et al., 2017).

The negative-sense RNAs are intermediate molecules produced by the replicase transcriptase complex (RTC) formed by the nonstructural proteins of coronaviruses (including SARS-CoV-2) to provide efficiency in replication and transcription (Bezzi et al., 2021; Sola et al., 2015).

This, however, introduces another potentially serious complication associated with vaccination. Co-infection with other negative sense RNA viruses such as hepatitis C (Jaubert et al., 2018) or infection by other coronaviruses contemporaneous with vaccination periods would provide the necessary machinery of RTC to reproduce negative sense intermediates from synthetic mRNAs and therefore amplify the presence of pG4s by negative sense templates. This would result in further epitranscriptomic dysregulation (Spiegel et al., 2020).

Summarizing the topic to this point, the enrichment of GC content in vaccine mRNA will inevitably lead to an increase in the pG4 content of the vaccines. This, in turn, will lead to dysregulation of the G4-RNA-protein binding system and a wide range of potential disease-associated cellular pathologies including suppression of innate immunity, neurodegeneration, and malignant transformation (Herdy et al., 2018).

Concerning the post translational dysregulation due to emergence of new G4 structures introduced by vaccination, one other important issue related to miRNA regulation and pG4s arises. In miRNA structures, hundreds of pG4 sequences are identified (Rouleau et al., 2018). In their unfolded conformation, as during binding to their respective targets in 3′ to 5′ sequences of mRNAs, miRNAs switch off the translation of their respective target mRNA. Alternatively, when in the presence of a G4 ligand, the translation of their target mRNAs is promoted (Chan et al., 2018). Moreover, a vast number of putative miRNA binding sites overlap with G4s in 3' UTRs of mRNAs as there are at least 521 specific miRNAs that are predicted to bind to at least one of these G4s. Overall, 44,294 potential G4-miRNA binding sites have been traced to possess putative overlapping G4s in humans (Rouleau et al., 2017).

As described elsewhere, during the cellular translation of vaccine mRNAs, an increased assembly of a number of RNA binding protein helicases, such as eIF4A bound to eIF4G, will occur (Kyriakopoulos and McCullough, 2021). The presence of increased pG4s in synthetic mRNAs can potentially amplify binding of RNA binding proteins and miRNAs. This form of molecular crowding of protein components (helicases) with great affinity for G4 binding (Rouleau et al., 2017) will decrease the number of RNA binding proteins binding G4s normally available for miRNA regulation. This loss of RNA binding proteins as well as miRNA availability for regulation by binding to G4s can dramatically alter the translational regulation of miRNAs present in cells and thereby disrupt essential regulation of oncogene expression. An example is the p16-dependent regulation of the p53 tumor suppressor protein (Rouleau et al., 2017; Al-Khalaf and Aboussekhra, 2018).

This process is exceedingly complicated yet tantamount to cellular homeostasis. So, again, it merits summarizing. If pG4s accumulate, as would be expected with an increased amount of GC content in the vaccine mRNA, this would have an effect of increasing potential G4 structures available during translation events and this can affect miRNA post-transcriptional regulation. This, in turn, would either favor greater expression of the oncogenes related to a range of cancers, or drive cells towards apoptosis and cell death (Weldon et al., 2018). The case study described earlier in this paper strongly supports the hypothesis that these injections induce accelerated lymphoma progression in follicular B-cells (Goldman et al., 2021).

miRNA binding recognition patterns are imperfectly complementary to their target regions, and for this reason they are referred to as "master regulators," since one miRNA affects a plethora of different targets (Rouleau et al., 2018). The multitude of pG4s in the mRNA of the vaccine would predictably act as decoys, distracting miRNAs from their normal function in regulating human protein expression. The increase in G4 targets due to the vaccine would decrease the availability of miRNAs to target human-expressed G4s for regulation of gene expression. This can result in downregulation of miRNA expression which is implicated in cardiovascular pathology (Small and Olson, 2011), onset of neurodegeneration (Abe and Bonini, 2013), and/or cancer progression (Farazi et al., 2013).

In most respects within epitranscriptomic machinery, miRNAs are involved in translation repression. One example, vital for cellular normal housekeeping, is that of Mouse double minute 2 homolog (MDM2), a physical negative regulatory protein of p53. P53 itself is considered the master regulator of the cellular tumor suppression network of genes. P16 controls the expression of many miRNAs, and, via miR-141 and mIR-146b-5p binding to MDM2 mRNA, it induces the negative regulation of MDM2, thus enabling p53 ubiquitination and promotion of cell survival upon DNA damage events (Al-Khalaf and Aboussekhra, 2018). Dysregulation of miRNAs that control MDM2 suppression of p53 would predictably lead to an increased risk to a range of cancers (Ozaki and Nakagawara, 2011).

5. Type I IFNs and COVID-19

Type I IFNs play an essential role in fighting viral infections, and deficiencies in type I IFN signaling have been associated with poor outcomes from COVID-19 in multiple studies. These cases are often associated with autoantibodies to type I IFNs. As reviewed below, type I IFNs have been used with some success in treating severe COVID-19, particularly if administered very early in the disease process. If, as argued above, the mRNA vaccines interfere with type I IFN signaling, this could lead to increased susceptibility to COVID-19 in the two weeks following the first vaccine, before an antibody response has been initiated.

Cells infected with a virus detect the presence of virus replication through a number of pattern recognition receptors (PRRs), which serve as sentinels sensing aberrant RNA structures that often form during viral replication. These receptors respond by oligomerizing and subsequently inducing type I IFNs, ultimately upregulating a large number of proteins involved in suppressing viral proliferation (Janeway and Medzhitov, 2002).

A multi-author study by researchers in Paris, France, involving a cohort of 50 COVID-19 patients with varying degrees of disease severity, revealed that patients with severe disease were characterized by a highly impaired type I IFN response (Hadjadj et al., 2020). These patients had essentially no IFN-β and low IFN-α production and activity. This was associated with a persistent blood viral load and an exacerbated inflammatory response, characterized by high levels of tumor necrosis factor α (TNF-α) and Il-6. The authors proposed type I IFN therapy as a potential treatment option. A paper by several researchers in the United States also identified a unique and inappropriate inflammatory response in severe COVID-19 patients, characterized by low levels of both type I and type III IFNs along with elevated chemokines and elevated expression of Il-6 (Blanco-Melo et al., 2020).

Type I IFNs have even been proposed as a treatment option for severe COVID-19. In a hamster model, researchers exposed hamsters to SARS-CoV-2 and induced an inflammatory response in the lungs and systemic inflammation in distal tissues. They found that intranasal administration of recombinant IFN-α resulted in a reduced viral load and alleviation of symptoms (Hoagland et al., 2021). A retrospective cohort study of 446 COVID-19 patients determined that early administration of IFN-α2b was associated with reduced in-hospital mortality. However, late IFN therapy increased mortality and delayed recovery, revealing that early administration of interferon therapy is essential for a favorable response (Wang et al., 2020a).

A surprising number of people have neutralizing autoantibodies against type I IFNs, although the underlying etiology of this phenomenon is not understood. A study using longitudinal profiling of over 600,000 peripheral blood mononuclear cells and transcriptome sequencing from 54 patients with COVID-19 and 26 controls found a notable lack of type I IFN-stimulated gene responses in myeloid cells from patients with critical disease (van der Wijst et al., 2021). Neutralizing autoantibodies against type I IFNs were found in 19% of patients with critical disease, 6% of patients with severe disease, and 0% of patients with moderate disease. Another study based in Madrid, Spain revealed that 10% of patients with severe COVID-19 disease had

autoimmune antibodies to type I IFNs (Troya et al., 2021). A multi-author study based in France found that COVID-19 mortality was significantly more frequent in patients with neutralizing autoantibodies against type I interferon than those without neutralizing antibodies (55% vs. 23%) (Chauvineau - Grenier et al., 2022). Finally, Stertz and Hale (2021) note that, whether due to autoantibodies or perhaps loss-of-function polymorphisms associated with interferon system genes, deficiencies in interferon production are associated with as many as 15% of all life-threatening COVID-19 cases.

6. Are the methylation strategies for cellular housekeeping generally omitted by vaccine mRNAs?

Methylation of mRNAs has been evolutionarily devised to control translation of transcripts and therefore expression of genes by a complex cascade of methylator (writers), de-methylator (eraser) and reader proteins. Adenosine methylation is the most abundant epitranscriptomic mRNA modification, and it occurs at multiple sites across the mRNA molecule (Zaccara et al., 2019). A key methylation of adenosine "N6-methyladenosine (m6A)" specifically in the 5′ UTR of mRNAs regulates normal cell physiology, the inflammatory response and cancer progression. The role and mechanisms of m6A in human disease is extensive, and it is excellently covered in other comprehensive reviews (Yang et al., 2020; Knuckles and Bühler, 2018). Foremost among these, the SARS-CoV-2 molecular vaccination induces cell stress conditions, as is described by the elevated NF-κB signaling after vaccination (Liu et al., 2021; Koo et al., 2010).

Under conditions of cellular stress, which can be induced by a viral infection or disease states such as cancer, m6A mediates mRNAs to undergo translation preferentially in a cap-independent way (Meyer et al., 2015). As discussed previously, this is opposite to the impact of mRNA SARS-CoV-2 vaccination, which drives cells toward a *cap-dependent* translation. Furthermore, under diversified conditions of cellular stress, there is an overwhelming induction of transcriptome-wide addition of m6A that causes an increased number of mRNAs to possess 5′UTRs enriched with m6A (Meyer et al., 2015).

Eukaryotic translation initiation factor 4E (eIF4E) is the initial mRNA cap-binding protein that directs ribosomes to the cap structure of mRNAs, in order to initiate translation into protein. The dependence on cap-dependent translation of vaccine mRNAs will consume a surplus of eIF4E availability needed to translate an unnaturally high number of synthetic mRNAs. However, cap-independent translation takes place without requiring eIF4E to be bound to eIF4F. The competition for ribosomes will shift towards the cap-independent translation of transcripts, since the mRNAs undergoing cap-independent translation are equipped, apart from internal ribosome entry sites (IRES), with special binding motifs that bind to factors that actively recruit mRNAs to the ribosome cap-independent translational enhancers (CITEs) (Shatsky et al., 2018).

Furthermore, this also means that eIF4E, which is a powerful oncogene regulator and cell proliferation modulator, will sustain its activities by this competition for an unnaturally prolonged period of time, trying to counterbalance the competition between robustly-capped mRNAs in vaccines and IRES-containing mRNAs (Kyriakopoulos and McCullough, 2021; Svitkin et al., 2005). This type of condition results in dysregulation of co-transcriptional m6A mRNA modifications and seriously links to molecular progressions of various cancers (Han and Choe, 2020), as well as creating predisposing conditions for subsequent viral infections (Svitkin et al., 2005).

We next consider the impact of mRNA-vaccination-derived SARS-CoV-2 spike glycoprotein on the cellular IFN system via massive exosome production.

7. Exosomes and MicroRNAs

An important communication network among cells consists of extracellular vesicles (EVs) that are constantly released by one cell and later taken up by another cell, which could be in a distant organ. Small vesicles known as exosomes, formed inside endosomes, are similar in size to viruses, and are released through exocytosis into the extracellular space to subsequently circulate throughout the body (Yoshikawa et al., 2019). Exosomes can deliver a diverse collection of biologically active molecules, including mRNA, microRNAs (miRNAs), proteins, and lipids (Ratajczak and Ratajczak, 2016). During a viral infection, infected cells secrete large quantities of exosomes that act as a communication network among the cells to orchestrate the response to the infection (Chahar et al., 2015).

In a collaborative effort by a team of researchers from Arizona and Connecticut, it was found that people who were vaccinated with the mRNA vaccines acquired circulating exosomes containing the SARS-CoV-2 spike glycoprotein by day 14 following vaccination (Bansal et al., 2021). They also found that there were no circulating antibodies to the spike glycoprotein fourteen days after the first vaccine. After the second vaccine, however, the number of circulating spike-glycoprotein-containing exosomes increased by up to a factor of 12. Furthermore, antibodies first appeared on day 14. The exosomes presented spike glycoprotein on their surface, which, the authors argued, facilitated antibody production. When mice were exposed to exosomes derived from vaccinated people, they developed antibodies to the spike glycoprotein. Interestingly, following peak expression, the number of circulating spike-glycoprotein-containing exosomes decreased over time, in step with the decrease in the level of antibodies to the spike glycoprotein.

Exosomes exist as a part of the mRNA decay mechanism in close association under stress conditions with stress granules (SGs) and P-bodies (PBs) (Decker and Parker, 2012; Kothandan et al., 2020). Under conditions of vaccine-mRNA-induced translation, which could be called "excessive dependence on cap-dependent translation," there is an obvious resistance to promotion and assembly of the large decapping complex (Kyriakopoulos and McCullough, 2021), and therefore resistance against physiological mRNA decay processes (Decker and Parker, 2012). This would mean that the fate of particular synthetic mRNAs that otherwise would be determined by the common cellular strategy for mRNA turnover involving messenger ribonucleinproteins (mRNPs) is being omitted (Borbolis and Syntichaki, 2015).

Furthermore, under conditions of over-reliance on cap-dependent translation by the synthetic mRNAs in SARS-CoV-2 vaccines (Kyriakopoulos and McCullough, 2021), many native mRNAs holding considerable IRES and specific methylations (m6A) in their structure will favorably choose cap-independent translation, which is strongly linked to mRNA decay quality control mechanisms (Han and Choe, 2020). In this sense, considerable deadenylated mRNA products as well as products derived from mRNA metabolism (decay) are directly linked to exosome cargoes (Borbolis and Syntichaki, 2015).

An example of dependence on cap-dependent translation is described in T-cell acute lymphoblastic leukaemia (T-ALL). Due to mechanistic target of rapamycin C (mTORC)-1 over-functioning in T-ALL, the cells are driven completely towards cap-dependent translation (Girardi and De Keersmaecker, 2015). An analogous condition is described by Kyriakopoulos and McCullough (2021). Even in this highly aggressive cancerous state, during inhibition of cap-dependent translation in T-ALL cells, there is a rapid reversion to cap-independent translation (Girardi and De Keersmaecker, 2015). Similarly, a picornavirus infection (Jang et al., 1990) drives cells towards cap-independent translation due to inhibition of components of eIF4F complex and pluralism of IRES in viral RNA.

In humans, there is an abundance of mostly asymptomatic picornavirus infections like the Safford Virus with an over 90% seroprevalence in young children and adults (Zoll et al., 2009). In either case, whether an apoptotic event due to a stress-like condition (Rusk, 2008) or an mRNA-cap-driven-like carcinomatous effect (De Paolis et al., 2021), the miRNA levels will be increased due to the increased epitranscriptomic

functioning and enhanced mRNA decay. Because of the high demand for gene expression, high levels of certain miRNAs will be expected to be contained in exosomes via P bodies (Yu et al., 2016).

Also, under conditions of overwhelming production of SARS-CoV-2 spike glycoprotein due to SARS-CoV-2 molecular vaccination, it would of course be expected that a significant proportion of over-abundant intracellular spike glycoproteins would also be exported via exosome cargoes (Wei et al., 2021).

Mishra and Banerjea (2021) investigated the role of exosomes in the cellular response of SARS-CoV-2 spike-transfected cells. They wrote in the abstract:

> "We propose that SARS-CoV-2 gene product, Spike, is able to modify the host exosomal cargo, which gets transported to distant uninfected tissues and organs and can initiate a catastrophic immune cascade within Central Nervous System (CNS)."

Their experiments involved growing human HEK293T cells in culture and exposing them to SARS-CoV-2 spike gene plasmids, which induced synthesis of spike glycoprotein within the cells. They found experimentally that these cells released abundant exosomes housing spike glycoprotein along with specific microRNAs. They then harvested the exosomes and transferred them to a cell culture of human microglia (the immune cells that are resident in the brain). They showed that the microglia readily took up the exosomes and responded to the microRNAs by initiating an acute inflammatory response. The role of microglia in causing neuroinflammation in various viral diseases, such as Human Immunodeficiency Virus (HIV), Japanese Encephalitis Virus (JEV), and Dengue, is well established. They proposed that long-distance cell-cell communication via exosomes could be the mechanism by which neurological symptoms become manifest in severe cases of COVID-19.

In further exploration, the authors identified two microRNAs that were present in high concentrations in the exosomes: miR-148a and miR-590. They proposed a specific mechanism by which these two microRNAs would specifically disrupt type I interferon signaling, through suppression of two critical proteins that control the pathway: ubiquitin specific peptidase 33 (USP33) and IRF9. Phosphorylated STAT1 and STAT2 heterodimers require IRF9 in order to bind IFN-stimulated response elements, and therefore IRF9 plays an essential role in the signaling response. The authors showed experimentally that microglia exposed to the exosomes extracted from the HEK293 culture had a 50% decrease in cellular expression of USP33 and a 60% decrease in IRF9. They further found that miR-148a specifically blocks USP33 and miR-590 specifically blocks IRF9. USP33 removes ubiquitin from IRF9, and in so doing it protects it from degradation. Thus, the two microRNAs together conspire to interfere with IRF9, thus blocking receptor response to type I interferons.

A study by de Gonzalo-Calvo et al. (2021) looked at the microRNA profile in the blood of COVID-19 patients and their quantitative variance based upon disease severity. Multiple miRNAs were found to be up- and down-regulated. Among these was miR-148a-3p, the guide strand precursor to miR-148a. However, miR-148a itself was not among the microRNAs catalogued as excessive or deficient in their study, nor was miR-590. It appears from these findings that miR148a and miR-590 and their inflammatory effects are unique to vaccination-induced SARS-CoV-2 spike glycoprotein production.

Tracer studies have shown that, following injection into the arm muscle, the mRNA in mRNA vaccines is carried into the lymph system by immune cells and ultimately accumulates in the spleen in high concentrations (Bahl et al., 2017). Other studies have shown that stressed immune cells in germinal centers in the spleen release large quantities of exosomes that travel to the brain stem nuclei along the vagus nerve (as reviewed in Seneff and Nigh (2021)). The vagus nerve is the 10th cranial nerve and it enters the brainstem near the larynx. The superior and recurrent laryngeal nerves are branches of the vagus that innervate structures involved in swallowing and speaking. Lesions in these nerves cause vocal cord paralysis associated with difficulty swallowing (dysphagia) difficulty speaking (dysphonia) and/or shortness of breath (dyspnea) (Gould et al., 2019; Erman et al., 2009). We will return to these specific pathologies in our review of VAERS data below.

HEK293 cells were originally derived from cultures taken from the kidney of a human fetus several decades ago and immortalized through infection with adenovirus DNA. While they were extracted from the kidney, the cells show through their protein expression profile that they are likely to be of neuronal origin (Shaw et al., 2002). This suggests that neurons in the vagus nerve would respond similarly to the SARS-CoV-2 spike glycoprotein. Thus, the available evidence strongly suggests that endogenously produced SARS-CoV-2 spike glycoprotein creates a different microRNA profile than does natural infection with SARS-CoV-2, and those differences entail a potentially wide range of deleterious effects.

A central point of our analysis below is the important distinction between the impact of vaccination versus natural infection on type I IFN. While vaccination actively suppresses its production, natural infection promotes type I IFN production very early in the disease cycle. Those with preexisting conditions often exhibit impaired type I IFN signaling, which leads to more severe, critical, and even fatal COVID-19. If the impairment induced by the vaccine is maintained as antibody levels wane over time, this could lead to a situation where the vaccine causes a more severe disease expression than would have been the case in the absence of the vaccine.

Another expected consequence of suppressing type I IFN would be reactivation of preexisting, chronic viral infections, as described in Section 9.

8. Impaired DNA repair and adaptive immunity

The immune system and the DNA repair system are the two primary systems that higher organisms rely on for defense against diverse threats, and they share common elements. Loss of function of key DNA repair proteins leads to defects in repair that inhibit the production of functional B- and T-cells, resulting in immunodeficiency. Non-homologous end joining (NHEJ) repair plays a critical role in lymphocyte-specific V(D)J recombination, which is essential for producing the highly diverse repertoire of B-cell antibodies in response to antigen exposure (Jiang and Mei, 2021). Impaired DNA repair is also a direct pathway towards cancer.

A paper published by Liu et al., in 2021 monitored several parameters associated with immune function in a cohort of patients by conducting single-cell mRNA sequencing of peripheral blood mononuclear cells (PBMCs) harvested from the patients before and 28 days after the first injection of a COVID-19 vaccine based on a weakened version of the virus (Liu et al., 2021). While these vaccines are different from the mRNA vaccines, they also work by injecting the contents of the vaccine into the deltoid muscle, bypassing the mucosal and vascular barriers. The authors found consistent alteration of gene expression following vaccination in many different immune cell types. Observed increases in NF-κB signaling and reduced type I IFN responses were further confirmed by biological assays. Consistent with other studies, they found that STAT2 and IRF7 were significantly downregulated 28 days after vaccination, indicative of impaired type I IFN responses. They wrote: "Together, these data suggested that after vaccination, at least by day 28, other than generation of neutralizing antibodies, people's immune systems, including those of lymphocytes and monocytes, were perhaps in a more vulnerable state." (Liu et al., 2021).

These authors also identified disturbing changes in gene expression that would imply impaired ability to repair DNA. Up to 60% of the total transcriptional activity in growing cells involves the transcription of ribosomal DNA (rDNA) to produce ribosomal RNA (rRNA). The enzyme that transcribes ribosomal DNA into RNA is RNA polymerase I (Pol I). Pol I also monitors rDNA integrity and influences cell survival (Kakarougkas et al., 2013). During transcription, RNA polymerases (RNAPs)

actively scan DNA to find bulky lesions (double-strand breaks) and trigger their repair. In growing eukaryotic cells, most transcription involves synthesis of ribosomal RNA by Pol I. Thus, Pol I promotes survival following DNA damage (Kakarougkas et al., 2013). Many of the downregulated genes identified by Liu et al. (2021) were linked to the cell cycle, telomere maintenance, and both promoter opening and transcription of POL I, indicative of impaired DNA repair processes.

One of the gene sets that were suppressed was due to "deposition of new CENPA [centromere protein A] containing nucleosomes at the centromere." Newly synthesized CENPA is deposited in nucleosomes at the centromere during late telophase/early G1 phase of the cell cycle. This points to arrest of the cell cycle in G1 phase as a characteristic feature of the response to the inactivated SARS-CoV-2 vaccine. Arrest of pluripotent embryonic stem cells in the G1 phase (prior to replication initiation) would result in impaired self-renewal and maintenance of pluripotency (Choi et al., 2013).

Two checkpoint proteins crucially involved in DNA repair and adaptive immunity are BRCA1 and 53BP1, which facilitate both homologous recombination (HR) and NHEJ, the two primary repair processes (Zhang and Powell, 2005; Panier and Boulton, 2014). In an *in vitro* experiment on human cells, the SARS-CoV-2 full-length spike glycoprotein was specifically shown to enter the nucleus and hinder the recruitment of these two repair proteins to the site of a double-strand break (Jiang and Mei, 2021). The authors summarized their findings by saying, "Mechanistically, we found that the spike protein localizes in the nucleus and inhibits DNA damage repair by impeding key DNA repair protein BRCA1 and 53BP1 recruitment to the damage site."

Another mechanism by which the mRNA vaccines could interfere with DNA repair is through miR-148. This microRNA has been shown to downregulate HR in the G1 phase of the cell cycle (Choi et al., 2014). As was mentioned earlier in this paper, this was one of the two microRNAs found in exosomes released by human cells following SARS-CoV-2 spike glycoprotein synthesis in the experiments by Mishra and Banerjea (2021).

9. Reactivation of varicella-zoster

Type I IFN receptor signaling in $CD8^+$ T cells is critical for the generation of effector and memory cells in response to a viral infection (Kolumam et al., 2005). $CD8^+$ T cells can block reactivation of latent herpes infection in sensory neurons (Liu et al., 2000). If type I IFN signaling is impaired, as happens following vaccination but not following natural infection with SARS-CoV-2, $CD8^+$ T cells' ability to keep herpes in check would also be impaired. Might this be the mechanism at work in response to the vaccines?

Shingles is an increasingly common condition caused by reactivation of latent herpes zoster viruses (HZV), which also causes chicken pox in childhood. In a systematic review, Katsikas Triantafyllidis et al. (2021) identified 91 cases of herpes zoster occurring an average of 5.8 days following mRNA vaccination. While acknowledging that causality is not yet confirmed, "Herpes zoster is possibly a condition physicians and other healthcare professionals may expect to see in patients receiving COVID-19 vaccines" (Katsikas Triantafyllidis et al., 2021). In a letter to the editor published in September 2, 2021, Fathy et al. (2022) reported on 672 cases of skin reactions that were presumably vaccine-related, including 40 cases of herpes zoster and/or herpes simplex reactivation. These cases had been reported to the American Academy of Dermatology and the International League of Dermatologic Societies' COVID-19 Dermatology Registry, established specifically to track dermatological sequalae from the vaccines. There are multiple additional case reports of herpes zoster reactivation following COVID-19 vaccination in the literature (Psichogiou et al., 2021b; Iwanaga et al., 2021). Lladó et al. (2021) noted that 51 of 52 reports of reactivated herpes zoster infections happened following mRNA vaccination. Herpes zoster itself also interferes with IFN-α signaling in infected cells both through interfering with STAT2 phosphorylation and through facilitating IRF9 degradation (Verweij et al., 2015).

An additional case of viral reactivation is noteworthy as well. It involved an 82-year-old woman who had acquired a hepatitis C viral (HCV) infection in 2007. A strong increase in HCV load occurred a few days after vaccination with an mRNA Pfizer/BioNTech vaccine, along with an appearance of jaundice. She died three weeks after vaccination from liver failure (Lensen et al., 2021).

10. Immune thrombocytopenia

Immune thrombocytopenia is an autoimmune disorder, where the immune system attacks circulating platelets. Immune thrombocytopenic purpura (ITP) has been associated with several vaccinations, including measles, mumps, rubella (MMR), hepatitis A, varicella, diphtheria, tetanus, pertussis (DPT), oral polio and influenza (Perricone et al., 2014). While there is broad awareness that the adenovirus DNA-based vaccines can cause vaccine-induced immune thrombotic thrombocytopenia (VITT) (Kelton et al., 2021), the mRNA vaccines are not without risk to VITT, as case studies have been published documenting such occurrences, including life threatening and fatal cerebral venous sinus thrombosis (Lee et al., 2021; Akiyama et al., 2021; Atoui et al., 2022; Zakaria et al., 2021). The mechanism is believed to involve VITT antibodies binding to platelet factor 4 (PF4) and forming immune complexes that induce platelet activation. Subsequent clotting cascades cause the formation of diffuse microclots in the brain, lungs, liver, legs and elsewhere, associated with a dramatic drop in platelet count (Kelton et al., 2021). The reaction to the vaccine has been described as being very similar to heparin-induced thrombocytopenia (HIT), except that heparin administration is notably not involved (Cines and Bussel, 2021).

It has been shown that the mRNA vaccines elicit primarily an immunoglobulin G (IgG) immune response, with lesser amounts of IgA induced (Wisnewski et al., 2021), and even less IgM production (Danese et al., 2021). The amount of IgG antibodies produced is comparable to the response seen in severe cases of COVID-19. It is IgG antibodies in complex with heparin that induce HIT. One can hypothesize that IgG complexed with the SARS-CoV-2 spike glycoprotein and PF4 is the complex that induces VITT in response to mRNA vaccines. It has in fact been shown experimentally that the receptor binding domain (RBD) of the spike protein binds to PF4 (Passariello et al., 2021).

The underlying mechanism behind HIT has been well studied, including through the use of humanized mouse models. Interestingly, human platelets, but not mouse platelets, express the FcγRIIA receptor, which responds to PF4/heparin/IgG complexes through a tyrosine phosphorylation cascade to induce platelet activation. Upon activation, platelets release granules and generate procoagulant microparticles. They also take up calcium, activate protein kinase C, clump together into microthrombi, and launch a cell death cascade via calpain activation. These activated platelets release PF4 into the extracellular space, supporting a vicious cycle, as this additional PF4 also binds to heparin and IgG antibody to further promote platelet activation. Thus, FcγRIIA is central to the disease process (Nevzorova et al., 2019).

Studies on mice engineered to express the human FcγRIIA receptor have shown that these transgenic mice are far more susceptible to thrombocytopenia than their wild type counterparts (McKenzie et al., 1999). It has been proposed that platelets may serve an important role in the clearance of antibody-antigen complexes by trapping the antigen in thrombi and/or carrying them into the spleen for removal by immune cells. Platelets are obviously rapidly consumed in the process, which then results in low platelet counts (thrombocytopenia).

Platelets normally circulate with an average lifespan of only five to nine days, so they are constantly synthesized in the bone marrow and cleared in the spleen. Antibody-bound platelets, subsequent to platelet activation via Fcγ receptors, migrate to the spleen where they are trapped and removed through phagocytosis by macrophages (Crow and Lazarus, 2003). Fully one third of the body's total platelets are found in the spleen. Since the mRNA vaccines are carried into the spleen by

immune cells initially attracted to the injection site in the arm muscle, there is tremendous opportunity for the release of spike-glycoprotein-containing exosomes by dendritic cells in the spleen synthesizing spike protein. One can speculate that platelet activation following the formation of a P4F/IgG/spike protein complex in the spleen is part of the mechanism that attempts to clear the toxic spike glycoprotein.

We mentioned earlier that one of the two microRNAs highly expressed in exosomes released by human cells exposed to the SARS-CoV-2 spike glycoprotein was miR-148a. miR-148a has been shown experimentally to suppress expression of a protein that plays a central role in regulating FcγRIIA expression on platelets. This protein, called T-cell ubiquitin ligand-2 (TULA-2), specifically inhibits activity of the platelet Fcγ receptor. miR-148a targets TULA-2 mRNA and downregulates its expression. Thus, miR-148a, present in exosomes released by macrophages that are compelled by the vaccine to synthesize SARS-CoV-2 spike glycoprotein, acts to increase the risk of thrombocytopenia in response to immune complexes formed by spike glycoprotein antigen and IgG antibodies produced against the spike glycoprotein.

11. PPAR-α, sulfatide and liver disease

As we have already stated, an experiment by Mishra and Banerjea (2021) demonstrated that the SARS-CoV-2 spike glycoprotein induces the release of exosomes containing microRNAs that specifically interfere with IRF9 synthesis. In this section we will show that one of the consequences of suppression of IRF9 would be reduced synthesis of sulfatide in the liver, mediated by the nuclear receptor peroxisome proliferator-activated receptor α (PPAR-α).

Sulfatides are major mammalian serum sphingoglycolipids which are synthesized and secreted mainly from the liver (Lu et al., 2019). They are the only sulfonated sphingolipids in the body. Sulfatides are formed by a two-step process involving the conversion of ceramide to galactocerebroside and its subsequent sulfation. Sulfatide is expressed on the surface of platelets, erythrocytes and lymphocytes. Serum sulfatides exert both anti-coagulative and anti-platelet-activation functions. The enzyme in the liver that synthesizes sulfatide, cerebroside sulfotransferase, has specifically been found to be induced by activation of PPAR-α in mice (Kimura et al., 2012). Therefore, reduced expression of PPAR-α leads to sulfatide deficiency.

PPAR-α ligands exhibit anti-inflammatory and anti-fibrotic effects, whereas PPAR-α deficiency leads to hepatic steatosis, steatohepatitis, steatofibrosis, and liver cancer (Wang et al., 2020b). In 2019, an experiment was conducted by a team of researchers in Japan on mice with a defective gene for PPAR-α (Lu et al., 2019). These mice, when fed a high cholesterol diet, were susceptible to excess triglyceride accumulation and exacerbated inflammation and oxidative stress in the liver, along with increased levels of coagulation factors. The mice also manifested with decreased levels of sulfatides in both the liver and the serum. The authors hypothesized that cholesterol overload exerts its toxic effects in part by enhancing thrombosis, following abnormal hepatic lipid metabolism and oxidative stress. They showed that PPAR-α can attenuate these toxic effects through transcriptional regulation of coagulation factors and upregulation of sulfatide synthesis, in addition to its effects in ameliorating liver disease. They proposed that therapies such as fibrates aimed at activating PPAR-α might prevent high-cholesterol-diet-induced cardiovascular disease.

Tracer studies have shown that the mRNA from mRNA vaccines migrates preferentially to the liver and spleen, reaching higher concentration there than in any other organs (Bahl et al., 2017). Thus, there is potential for suppression of IRF9 in the liver by the vaccine. IRF9 is highly expressed in hepatocytes, where it interacts with PPAR-α, activating PPAR-α target genes. A study on IRF9 knockout mice showed that these mice developed steatosis and hepatic insulin resistance when exposed to a high-fat diet. In contrast, adenoviral-mediated hepatic IRF9 overexpression in obese mice improved insulin sensitivity and ameliorated steatosis and inflammation (Wang et al., 2013).

Multiple case reports in the research literature describe liver damage following mRNA vaccines (Zin Tun et al., 2021; Dumortiera, 2022; Mann et al., 2021). A plausible factor leading to these outcomes is the suppression of PPAR-α through downregulation of IRF9, and subsequently decreased sulfatide synthesis in the liver.

12. Guillain Barré syndrome and neurologic injury syndromes

GBS is an acute inflammatory demyelinating neuropathy associated with long-lasting morbidity and a significant risk of mortality (Cr é ange, 2000). The disease involves an autoimmune attack on the nerves associated with the release of pro-inflammatory cytokines.

GBS is often associated with autoantibodies to sulfatide and other sphingolipids (Ilyas et al., 1991). Activated T-cells produce cytokines in response to antigen presentation by macrophages, and these cytokines can induce autoantibody production through epitope spreading (Vanderlugt and Miller, 2002). The antibodies, in turn, induce complement activation, which causes demyelination and axonal damage, leading to severe injury to peripheral neurons (Kuwahara and Kusunoki, 2018). The SARS-CoV-2 spike glycoprotein has been shown to bind to heparan sulfate, which is a sulfated amino-sugar complex resembling the sulfated galactose in sulfatide (Kalra and Kandimalla, 2021). Thus, it is conceivable that the spike glycoprotein also binds to sulfatide, and this might trigger an immune reaction to the spike-glycoprotein-sulfatide complex.

As described in the previous section, impaired sulfatide synthesis in the liver due to suppression of IRF9 will lead to systemic sulfatide deficiency over time. Sulfatide deficiency can have major impact in the brain and nervous system. Twenty percent of the galactolipids found in the myelin sheath are sulfatides. Sulfatide is a major component of the nervous system, found in especially high concentrations in the myelin sheath in both the peripheral and the central nervous system. Deficiencies in sulfatide can lead to muscle weakness, tremors, and ataxia (Honke, 2013), which are common symptoms of GBS. Chronic neuroinflammation mediated by microglia and astrocytes in the brain leads to dramatic losses of brain sulfatide, and brain deficiencies in sulfatide are a major feature of Alzheimer's disease (Qiu et al., 2021). Mice with a defect in the ability to synthesize sulfatide from ceramide show an impaired ability to maintain the health of axons as they age. Over time, they develop redundant, uncompacted and degenerating myelin sheaths as well as deteriorating structure at the nodes of Ranvier in the axons, causing the loss of a functionally competent axoglial junction (Marcus et al., 2006).

Angiotensin II (Ang II), in addition to its profound effects on cardiovascular disease, also plays a role in inflammation in the brain leading to neurodegenerative disease (Lanz. et al., 2010). The SARS-CoV-2 spike glycoprotein contains a unique furin cleavage site not found in SARS-CoV, which allows the extracellular enzyme furin to detach the S1 segment of the spike glycoprotein and release it into circulation (Letarov et al., 2021). S1 has been shown to cross the blood-brain barrier in mice (Rhea et al., 2021). S1 contains the receptor binding domain that binds to ACE2 receptors, disabling them. When ACE2 receptor signaling is reduced, Ang II synthesis is increased. Neurons in the brain possess ACE2 receptors that would be susceptible to disruption by S1 released from spike-glycoprotein-containing exosomes or spike-glycoprotein-producing cells that had taken up the nanoparticles in the vaccines. Ang II enhances TLR4-mediated signaling in microglia, inducing microglial activation and increasing the production of reactive oxygen species leading to tissue damage, within the paraventricular nucleus in the brain (Rodriguez-Perez et al., 2015).

Elevated levels of Ang II is a causal factor in neurodegeneration of the optic nerve, causing optic neuritis, which can result in severe irreversible visual loss (Guo et al., 2017). Multiple case reports have described cases of optic neuropathy appearing shortly after mRNA vaccination for COVID-19 (Maleki, 2021; Barone et al., 2021). Other

debilitating neurological conditions are also appearing shortly after vaccination, where a causal relationship is suspected. A case study based in Europe tracking neurological symptoms following COVID-19 vaccination identified 21 cases developing within a median of 11 days post-vaccination. The cases had diverse diagnoses including cerebral venous sinus thrombosis, nervous system demyelinating diseases, inflammatory peripheral neuropathies, myositis, myasthenia, limbic encephalitis, and giant cell arteritis (Kaulen et al., 2021). Khayat-Khoei et al. (2021) describe a case series of 7 patients, ages ranging from 24 to 64, presenting with demyelinating disease within 21 days of a first or second mRNA vaccination. Four had a prior history of (controlled) MS, while three were previously healthy.

Hearing loss and tinnitus are also well-known side effects of COVID-19. A case study involved a series of ten COVID-19 patients who suffered from audiovestibular symptoms such as hearing loss, vestibular dysfunction and tinnitus (Jeong et al., 2021). The authors demonstrated that human inner ear tissue expresses ACE2, furin and the transmembrane protease serine 2 (TMPRSS2), which facilitates viral entry. They also showed that SARS-CoV-2 can infect specific human inner ear cell types.

Another study evaluating the potential for the SARS-CoV-2 virus to infect the ear specifically examined expression of the receptor ACE2 and the enzymes furin and TM-PRSS2 various types of cells in the middle and inner ears of mice. They found that ACE2 and furin were "diffusely present in the eustachian tube, middle ear spaces, and cochlea, suggesting that these tissues are susceptible to SARS-CoV-2 infection." (Uranaka et al., 2021). Tinnitus is positively associated with hypertension, which is induced by elevated levels of Ang II (Rodrigues Figueiredo et al., 2016).

Headache is a very common adverse reaction to the COVID-19 mRNA vaccines, particularly for people who are already susceptible to headaches. In a study based on a questionnaire involving 171 participants, the incidence of headaches was found to be 20.5% after the first vaccine, rising to 45.6% after the second shot (Sekiguchi et al., 2021). A case study described a 37-year-old woman suffering from a debilitating migraine attack lasting for 11 days following the second Pfizer/BioNtech mRNA vaccine (Consoli et al., 2021).

Steroids are often used as adjunct therapy to treat migraine (Huang et al., 2013). Dexamethasone and other steroids stimulate PPAR-α receptors in the liver through the steroid receptor, thus offsetting the effects of IRF9 suppression (Lemberger et al., 1994). A theory for the origins of migraine involves altered processing of sensory input in the brainstem, primarily trigeminal neurons (Dodick and Silberstein, 2006). The trigeminal nerve is in close proximity to the vagus nerve in the brainstem, so spike-glycoprotein-carrying exosomes could easily reach it along the vagal route. Magnetic resonance imaging has revealed that structural changes in the trigeminal nerve reflecting aberrant microstructure and demyelination are a characteristic feature of people who suffer from frequent migraine headaches (Mungoven et al., 2020). A potential factor linked to either SARS-CoV-2 infection or mRNA vaccination is an excessive level of Ang II in the brainstem due to SARS-CoV-2 spike glycoprotein inhibition of ACE2 receptors. ACE inhibitors and Ang II receptor antagonists have become popular drugs to treat migraine headaches off-label (Tronvik et al., 2003; Nandha and Singh, 2012). Migraine headache could thus arise from both the spike glycoprotein's disruption of ACE2 receptors and the destruction of the myelin sheath covering critical facial nerves through a microglial inflammatory response and loss of sulfatide. The source of that spike glycoprotein could be either exogenous or endogenous.

13. Bell's palsy

Bell's palsy is a common cranial neuropathy causing unilateral facial paralysis. Even in the Phase III clinical trials, Bell's palsy stood out, with seven cases appearing in the treatment arm as compared to only one in the placebo group (FDA, 2021a; FDA, 2021b). A case study reported in the literature involved a 36-year-old man who developed weakness in the left arm one day after vaccination, progressing to numbness and tingling in the arm and subsequent symptoms of Bell's palsy over the next few days. A common cause of Bell's palsy is reactivation of herpes simplex virus infection centered around the geniculate ganglion (Eviston et al., 2015). This, in turn, can be caused by disruption of type I IFN signaling.

14. Myocarditis

There has been considerable media attention devoted to the fact that COVID-19 vaccines cause myocarditis and pericarditis, with an increased risk in particular for men below the age of 50 (Simone et al., 2021; Jain et al., 2021). The SARS-CoV-2 spike glycoprotein has been demonstrated to injure cardiac pericytes, which support the capillaries and the cardiomyocytes (Avolio et al., 2020). Myocarditis is associated with platelet activation, so this could be one factor at play in the response to the vaccines (Weikert. et al., 2002). However, another factor could be related to exosomes released by macrophages that have taken up the mRNA nanoparticles, and the specific microRNAs found in those exosomes.

A study involving patients suffering from severe COVID-19 disease looked specifically at the expression of circulating microRNAs compared to patients suffering from influenza and to healthy controls. One microRNA that was consistently upregulated in association with COVID-19 was miR-155, and the authors suggested that it might be a predictor of chronic myocardial damage and inflammation. By contrast, influenza infection was not associated with increased miR-155 expression. They concluded: "Our study identified significantly altered levels of cardiac-associated miRs [microRNAs] in COVID-19 patients indicating a strong association of COVID-19 with cardiovascular ailments and respective biomarkers" (Garg et al., 2021).

A study comparing 300 patients with cardiovascular disease to healthy controls showed a statistically significant increase in circulating levels of miR-155 in the patients compared to controls. Furthermore, those with more highly constricted arteries (according to a Gensini score) had higher levels than those with lesser disease (Qiu and Ma, 2018).

Importantly, exosomes play a role in inflammation in association with heart disease. During myocardial infarction, miR-155 is sharply upregulated in macrophages in the heart muscle and released into the extracellular milieu within exosomes. These exosomes are delivered to fibroblasts, and miR-155 downregulates proteins in the fibroblasts that protect from inflammation and promote fibroblast proliferation. The resulting impairment leads to cardiac rupture (Wang et al., 2017b).

We have already discussed how the S1 segment of the SARS-CoV-2 spike glycoprotein can be cleaved by furin and released into circulation. It binds to ACE2 receptors through its receptor binding domain (RBD), and this inhibits their function. Because ACE2 degrades Ang II, disabling ACE2 leads directly to overexpression of Ang II, further enhancing risk to cardiovascular disease. AngII-induced vasoconstriction is an independent mechanism to induce permanent myocardial injury even when coronary obstruction is not present. Repeated episodes of sudden constriction of a cardiac artery due to Ang II can eventually lead to heart failure or sudden death (Gavras and Gavras, 2002). Fatal cases of COVID-19 vaccination have been described (Choi et al., 2021; Verma et al., 2021).

ACE2 suppression had already been seen in studies on the original SARS-CoV virus. An autopsy study on patients succumbing to SARS-CoV revealed an important role for ACE2 inhibition in promoting heart damage. SARS-CoV viral RNA was detected in 35% of 20 autopsied human heart samples taken from patients who died. There was a marked increase in macrophage infiltration associated with myocardial damage in the patients whose hearts were infected with SARS-CoV. Importantly, the presence of SARS-CoV in the heart was associated with marked reduction in ACE2 protein expression (Oudit et al., 2009).

15. Considerations regarding the Vaccine Adverse Event Reporting System (VAERS)

The Food and Drug Administration's Vaccine Adverse Event Reporting System (VAERS) is an imperfect but valuable resource for identifying potential adverse reactions to vaccines. Established through collaboration between the CDC and FDA, VAERS is "a national early warning system to detect possible safety problems in U.S.-licensed vaccines." According to the CDC it is "especially useful for detecting unusual or unexpected patterns of adverse event reporting that might indicate a possible safety problem with a vaccine." (https://vaers.hhs.gov/about.html) Even the CDC recognizes that adverse events reported to VAERS represent "only a small fraction of actual adverse events" (Vaers Home, 2021). A widely cited report noted that fewer than 1% of all vaccine-related adverse events are reported to VAERS (Lazarus et al., 2010). That assertion, though, has no citation so the basis for the claim is unclear. Rose (2021) published a much more sophisticated analysis of VAERS data to offer an estimate of underreporting by a factor of 31 (Rose, 2021). While it is impossible to determine underreporting with precision, the available evidence is that underreporting very strongly characterizes the VAERS data. The information presented below should be understood in that light.

In mining VAERS for 'signals' that might indicate adverse reactions (AEs) to mRNA vaccinations, we acknowledge that no report to VAERS establishes a causal link with the vaccination. That said, the possibility of a causal relationship is strengthened through both the causal pathways we have described in this paper, and the strong temporal association between injections and reported AEs. Nearly 60% of all mRNA-injection-related -AEs have happened within 48 h of injection (https://medalerts.org/vaersdb/findfield.php?TABLE=ON&GROUP1=ONS&EVENTS=ON&VAX=COVID19&VAXTYPES=COVID-19&STATE=NOTFR).

Two important cautions regarding analysis of VAERS data should be noted. The first is that, in addition to health care professionals submitting reports, VAERS is open for public submissions as well. Members of the public may lack the skills necessary to evaluate a symptom appropriately to determine if it merits a VAERS entry. A second caution is that public access also allows for the possibility of anti-vaccination activists to populate VAERS with false reports to exaggerate the appearance of AE risk.

An interim analysis of deaths cited previously found that health service employees were the VAERS reporter in 67% of reports analyzed (Nandha and Singh, 2012), suggesting a large portion of VAERS reports are submitted by medical professionals and not the public. This finding also belies the notion that anti-vaccination activists are filing an excessive number of egregious reports of vaccine injury.

All of the data reported in this section were obtained by querying the online resource, http://wonder.cdc.gov/vaers.html. Over the 31-year history of VAERS, up to February 3, 2022, there were a total of 10,321 deaths reported as a "symptom" in association with any vaccine, and 8,241 (80%) of those deaths were linked to COVID-19 vaccines. Importantly, only 14% of COVID-19 VAERS-reported deaths as of June 2021 could have vaccination ruled out as a cause (McLachlan et al., 2021). This strongly suggests that these unprecedented vaccines exhibit unusual mechanisms of toxicity that go well beyond what is seen with more traditional vaccines.

We decided that a reasonable way to characterize the significance of adverse events linked to COVID-19 vaccines was to focus on events received in the year 2021, and to compare the counts in the "SYMPTOM" field for the events associated with COVID-19 vaccines to the total counts for that same symptom for all vaccines over that same year. In total, there were 737,689 events reported in VAERS for COVID-19 vaccines in 2021, representing a shocking 93% of the total cases reported for any vaccine that same year. While we recognize that some of the COVID-19 vaccines are based on DNA vector technology rather than mRNA technology, this class (i.e., the Johnson & Johnson vaccine) represents less than 9% of the COVID-19 reports, and its reaction profile is surely much more similar to that of the mRNA vaccines than to that of all the other vaccines.

The total number of adverse event reports for COVID-19 injections is far greater than the cumulative number of annual vaccine adverse event reports combined in all prior years, as shown by Rose (2021). The influenza vaccine is a good one to compare against. Given that the protocol for the mRNA vaccines requires two doses, and that many were persuaded to receive a booster shot as well, it is clear that the sheer number of COVID-19 vaccines administered is large compared to other vaccines. We can actually estimate what percent of the adverse reactions in 2021 would be expected to be associated with COVID-19 vaccines if the likelihood of an adverse reaction were similar to that of the influenza vaccine. The CDC tells us that 52% of the US population received a flu shot in 2021. The USAFacts web site provides percentages of the US population that received one, two or three doses of COVID-19 vaccines as a function of time (see: https://usafacts.org/visualizations/covid-vaccine-tracker-states/). The numbers they report for December 30, 2021 are 73% single dose, 62% fully vaccinated, and 21% boosted. This tallies up to 156% of the population as the total number of COVID-19 vaccines administered. This is exactly three times as many COVID vaccines as flu shots.

From VAERS, one can easily obtain the total number of adverse reactions associated with COVID-19 vaccines, the total number associated with flu vaccines, and the total number associated with all vaccines, for the US-restricted VAERS data from 2021. These come out as: COVID-19: 737,587, FLU: 9,124, and ALL: 792,935. First, we can observe that 93% of all the events reported were linked to COVID-19 vaccines. If we remove the counts for COVID-19 and replace them with three times the counts for flu (since COVID-19 vaccines were administered three times as often), we find that COVID-19 should have accounted for 32.6% of all the events, which can be compared with the actual result, which is 93%. We can also conclude that any event that shows up more than 93% as often for COVID-19 vaccines as for all other vaccines is especially significant as a potential toxic effect of these vaccines. Finally, we find that there are 27 times as many reports for COVID-19 vaccines as would be expected if its adverse reactions were comparable to those from the flu vaccine.

Table 1
Number of symptoms reported in VAERS, restricted to the US population, for the year 2021, for various adverse effects that could be caused by inflammation in associated major nerves, showing total counts for COVID-19 vaccines and for all vaccines.

Symptom	Inflamed Nerve(s)	Covid-19 Vaccines	All Vaccines	Percent COVID-19
Anosmia	olfactory nerve	3,657	3,677	99.5
Tinnitus	vestibulo-cochlear nerve	13,275	13,522	98.2
Deafness	cochlea	2,895	3,033	95.5
Bell's Palsy/ facial palsy	facial nerve	5,881	6,129	96.0
Vertigo	vestibular nerve	7,638	7,819	97.7
Migraine headache	trigeminal nerve	8,872	9,059	97.9
Dysphonia	glossopharyngeal nerve	1,692	1,751	96.6
Dysphagia	several lower cranial nerves	4,711	4,835	97.4
Nausea	vagus nerve	69,121	71,275	97.0
Vomiting	vagus nerve	27,885	28,955	96.3
Dyspnea	vagus nerve	39,551	40,387	97.9
Syncope	vagus nerve	14,701	15,268	96.3
Bradycardia	vagus nerve	673	699	96.3
TOTAL	**–**	**200,552**	**206,409**	**97.2**

15.1. VAERS data indicative of nerve damage and vagus nerve involvement

Table 1 lists a number of symptoms in VAERS that can be associated with inflammation of or damage to various major nerves of the body, particularly those in the head. Strikingly, COVID-19 vaccines represented from 96 to 98% of the reports in the year 2021 related to each of these debilitating conditions. There were nearly 100,000 cases of nausea or vomiting, which are common symptoms of vagus nerve stimulation or damage (Babic and Browning, 2014). 14,701 cases of syncope linked to COVID-19 vaccines represented 96.3% of all cases of syncope, a well-established feature of vagus nerve dysfunction (Fenton et al., 2000). There were 3,657 cases of anosmia (loss of smell), clearly demonstrating that the SARS-CoV-2 spike glycoprotein from the injection in the arm was reaching the olfactory nerve. Dyspnea (shortness of breath) is related to vagus nerve impairment in the lungs, and there were 39,551 cases of dyspnea connected to COVID-19 vaccines in 2021.

Altogether, these events add up to a total of over 200,000 events, representing 97.2% of all the entries related to any vaccine in 2021. This is also a substantial 27.2% of all the events listed for 2021 in association with COVID-19 vaccines.

15.2. VAERS data on the heart and liver

In this paper, we have identified both the heart and the liver as organs that can be expected to be affected by the mRNA vaccines. The VAERS database shows a strong signal for both organs. Table 2 shows the statistics for 2021 on major disorders of the heart, including myocarditis, arrest (cardiac, cardiorespiratory and sinus arrest), arrhythmia (including supraventricular, nodal, sinus, tachyarrhythmia and ventricular arrhythmia), myocardial infarction (including acute and silent), and cardiac failure (including acute, chronic and congestive). Altogether, there were a total of 8,090 COVID-19 events related to these heart conditions, representing nearly 98% of all the events for all the vaccines for these symptoms in 2021.

It is difficult to find all of the symptoms associated with liver damage in VAERS, but we selected a number that had high enough counts to be of interest and that clearly represent serious liver problems. Altogether there were 731 events in these categories for COVID-19 vaccines, as shown in Table 3, representing over 97% of all the cases connecting these conditions to any vaccine in 2021.

15.3. VAERS data related to thrombosis

There were 78 unique symptoms in VAERS involving thrombosis, specifying different arteries and veins. Table 4 shows nine symptoms with the highest counts, totaling 7,356 events. We investigated the time interval for the three dominant ones (thrombosis, deep vein thrombosis and pulmonary thrombosis), and found that these all have a sharp peak in the 15-30-day range for onset interval (time after vaccination). This coincides with a sharp peak in pulmonary embolism, a life-threatening condition, also in the 15-30-day time interval. Overall, for these nine thrombotic symptoms, a random sampling from the year 2021 would yield a COVID vaccine as opposed to any other vaccine 98.7% of the time. Pulmonary embolism, a life-threatening condition that can be caused by a blood clot that travels to the lungs, has a slightly higher probability of 98.8%, with 3,100 cases listed for COVID-19.

Table 2
Number of symptoms reported in VAERS, restricted to the US population, for the year 2021, for various disorders of the heart, showing total counts for COVID-19 vaccines and for all vaccines.

Symptom	Covid-19 Vaccines	All Vaccines	Percent COVID-19
Myocarditis	2,322	2,361	98.3
Arrest	1,319	1,371	96.2
Arrhythmia	1,069	1,087	98.3
Myocardial infarction	2,224	2,272	97.9
Cardiac failure	1,156	1,190	97.1
TOTAL	8,090	8,281	97.7

Table 3
Number of symptoms reported in VAERS, restricted to the US population, for the year 2021, for various indicators of liver disease, showing total counts for COVID-19 vaccines and for all vaccines.

Symptom	Covid-19 Vaccines	All Vaccines	Percent COVID-19
Liver disorder	83	87	95.4
[Drug-induced] liver injury	65	65	100
[Acute] hepatic failure	86	88	97.7
Hepatic cancer [metastatic]	12	12	100
Hepatic cirrhosis	67	69	97.1
Hepatic cyst	33	34	97.0
Liver function test increased	238	245	97.1
Liver function test abnormal	90	94	95.7
Hepatic function abnormal	34	34	100
Haemangioma of liver	10	10	100
Liver abscess	7	7	100
Liver transplant	6	6	100
TOTAL	**731**	**751**	**97.3**

Table 4
Number of symptoms reported in VAERS, restricted to the US population, for the year 2021, for various specific types of thrombosis, showing total counts for COVID-19 vaccines and for all vaccines. Pulmonary embolism, a highly related symptom, is also shown.

Symptom	Covid-19 Vaccines	All Vaccines	Percent COVID-19
Thrombosis	3,899	3,951	98.7
Deep vein thrombosis	2,275	2,297	99.0
Pulmonary thrombosis	631	646	97.7
Cerebral thrombosis	211	215	98.1
Portal vein thrombosis	89	90	98.9
Superficial vein thrombosis	81	81	100
Peripheral artery thrombosis	74	74	100
Mesenteric vein thrombosis	55	56	98.2
Venous thrombosis	41	41	100
TOTAL	**7,356**	**7,451**	**98.7**
Pulmonary embolism	**3,100**	**3,137**	**98.8**

15.4. VAERS data related to neurodegenerative disease

Table 5 lists results for several conditions that are linked to neurodegenerative disease. Decreased mobility can be caused by Parkinson's disease, and there were a striking 8,975 cases listed for 2021 and COVID-19 vaccines. Alzheimer's and Parkinson's are diseases that normally

Table 5
Number of symptoms reported in VAERS, restricted to the US population, for the year 2021, for various disorders linked to neurodegenerative disease, showing total counts for COVID-19 vaccines and for all vaccines.

Symptom	Covid-19 Vaccines	All Vaccines	Percent COVID-19
Alzheimer's dementia	37	39	94.9
Parkinsonian symptoms	83	89	93.3
Memory impairment	1,681	1,720	97.7
Anosmia	3,657	3,677	99.5
Mobility decreased	8,975	9,743	92.1
Cognitive disorder	779	815	92.1
TOTAL	**15,212**	**16,083**	**94.6**

take decades to develop, and ordinarily one would assume that a vaccine has nothing to do with it. While the numbers are small, most of the cases in VAERS were linked to COVID-19 vaccines. Anosmia, also included in the table on the vagus nerve, is especially interesting, because it is a well-known early sign of Parkinson's disease, and it is also a well-identified feature of SARS-CoV-2 infection. 99.5% of the cases with anosmia as a symptom were linked to COVID-19 vaccines. Overall, the symptoms in this table were linked to COVID-19 vaccines nearly 95% of the time.

15.5. VAERS signal for cancer

Cancer is a disease generally understood to take months or, more commonly, years to progress from an initial malignant transformation in a cell to development of a clinically recognized condition. Since VAERS reports of adverse events are happening primarily within the first month or even the first few days after vaccination (Rose, 2021), it seems likely that the acceleration of cancer progression following vaccines would be a difficult signal to recognize. Furthermore, most people do not expect cancer to be an adverse event that could be caused by a vaccine, and hence they fail to enter a report when cancer develops shortly after vaccination. However, as we have outlined in our paper, if the mRNA vaccinations are leading to widespread dysregulation of oncogene controls, cell cycle regulation, and apoptosis, then VAERS reports should reflect an increase in reports of cancer, relative to the other vaccines, even if the numbers are small. The experiment demonstrating impairment of DNA repair mechanisms by SARS-CoV-2 spike protein in an *in vitro* study provides compelling evidence that the vaccines could accelerate the rate of DNA mutations, increasing cancer risk (Jiang and Mei, 2021).

For our analysis of evidence of increased cancer risk in VAERS, we focused on two somewhat distinct approaches. One, represented by the results in Table 6, was to gather the counts for any terms that contained keywords clearly linked to cancer, namely, "cancer," "lymphoma," "leukaemia," "metastasis," "carcinoma," and "neoplasm." Overall, we found 1,474 entries linking these terms to COVID-19 vaccines, representing 96% of all the entries for any of these terms for any vaccine in that year.

The complementary approach was to find terms involving cancer in specific organs, namely, breasts, prostate, bladder, colon, brain, lungs, pancreas and ovaries, as shown in Table 7. Although all the numbers are small, the highest by far was for breast cancer (246 cases), with nearly four times as many hits as for lung cancer, the second most common type. All of the cases for pancreatic, ovarian and bladder cancer were linked to COVID-19 vaccines, with zero cases for any other vaccine. Altogether, we tabulated 534 cases of cancer of specific organs linked to COVID-19 vaccines, representing 97.3% of all the cases for any vaccine in 2021.

Table 6
Number of symptoms reported in VAERS, restricted to the US population, for the year 2021, for various cancer-related terms, showing total counts for COVID-19 vaccines and for all vaccines.

Symptom	Counts COVID-19 vaccines	Counts All Vaccines	Percent COVID-19
Cancer	396	403	98.3
Lymphoma	144	153	94.1
Leukaemia	155	161	96.3
Metastatic/ metastasis	175	179	97.8
Carcinoma	176	187	94.1
Neoplasm	428	452	94.7
TOTAL	**1,474**	**1,535**	**96.0**

Table 7
Number of symptoms reported in VAERS, restricted to the US population, for the year 2021, for cancer of specific organs, showing total counts for COVID-19 vaccines and for all vaccines.

Symptom	Counts COVID-19 vaccines	Counts All Vaccines	Percent COVID-19
Breast cancer	246	254	96.8
Prostate cancer	50	52	96.2
Bladder cancer	30	30	100
Colon cancer	40	41	97.6
Brain neoplasm	53	55	96.4
Lung cancer	64	66	97.0
Pancreatic cancer	24	24	100
Ovarian cancer	27	27	100
Total	**534**	**549**	**97.3**

16. Conclusions

There has been an unwavering message about the safety and efficacy of mRNA vaccinations against SARS-CoV-2 from the public health apparatus in the US and around the globe. The efficacy is increasingly in doubt, as shown in a recent letter to the Lancet Regional Health by Günter Kampf (2021b). Kampf provided data showing that the vaccinated are now as likely as the unvaccinated to spread disease. He concluded: "It appears to be grossly negligent to ignore the vaccinated population as a possible and relevant source of transmission when deciding about public health control measures." Moreover, the inadequacy of phase I, II, and III trials to evaluate mid-term and long-term side effects from mRNA genetic vaccines may have been misleading on their suppressive impact on the innate immunity of the vaccinees.

In this paper, we call attention to three very important aspects of the safety profile of these vaccinations. First is the extensively documented subversion of innate immunity, primarily via suppression of IFN-α and its associated signaling cascade. This suppression will have a wide range of consequences, not the least of which include the reactivation of latent viral infections and the reduced ability to effectively combat future infections. Second is the dysregulation of the system for both preventing and detecting genetically driven malignant transformation within cells and the consequent potential for vaccination to promote those transformations. Third, mRNA vaccination potentially disrupts intracellular communication carried out by exosomes, and induces cells taking up spike glycoprotein mRNA to produce high levels of spike-glycoprotein-carrying exosomes, with potentially serious inflammatory consequences. Should any of these potentials be fully realized, the impact on billions of people around the world could be enormous and could contribute to both the short-term and long-term disease burden our health care system faces.

Given the current rapidly expanding awareness of the multiple roles of G4s in regulation of mRNA translation and clearance through stress granules, the increase in pG4s due to enrichment of GC content as a consequence of codon optimization has unknown but likely far-reaching consequences. Specific analytical evaluation of the safety of these constructs in vaccines is urgently needed, including mass spectrometry for identification of cryptic expression and immunoprecipitation studies to evaluate the potential for disturbance of or interference with the essential activities of RNA and DNA binding proteins.

It is essential that further studies be conducted to determine the extent of the potential pathological consequences outlined in this paper. It is not practical for these vaccinations to be considered part of a public health campaign without a detailed analysis of the human impact of the potential collateral damage. VAERS and other monitoring systems should be optimized to detect signals related to the health consequences of mRNA vaccination we have outlined. We believe the upgraded VAERS monitoring system described in the Harvard Pilgrim Health Care, Inc. study, but unfortunately not supported by the CDC, would be a valuable start in this regard (Lazarus et al., 2010).

In the end, billions of lives are potentially at risk, given the large number of individuals injected with the SARS-CoV-2 mRNA vaccines and the broad range of adverse outcomes we have described. We call on the public health institutions to demonstrate, with evidence, why the issues discussed in this paper are not relevant to public health, or to acknowledge that they are and to act accordingly. Furthermore, we encourage all individuals to make their own health care decisions with this information as a contributing factor in those decisions.

Author contributions

S.S., G.N and A.K. all contributed substantially to the writing of the original draft. P.M. participated in the process of editorial revisions.

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Editorial

COVID UPDATE: What is the truth?

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The COVID-19 pandemic is one of the most manipulated infectious disease events in history, characterized by official lies in an unending stream lead by government bureaucracies, medical associations, medical boards, the media, and international agencies.[3,6,57] We have witnessed a long list of unprecedented intrusions into medical practice, including attacks on medical experts, destruction of medical careers among doctors refusing to participate in killing their patients and a massive regimentation of health care, led by non-qualified individuals with enormous wealth, power and influence.

For the first time in American history a president, governors, mayors, hospital administrators and federal bureaucrats are determining medical treatments based not on accurate scientifically based or even experience based information, but rather to force the acceptance of special forms of care and "prevention"—including remdesivir, use of respirators and ultimately a series of essentially untested messenger RNA vaccines. For the first time in history medical treatment, protocols are not being formulated based on the experience of the physicians treating the largest number of patients successfully, but rather individuals and bureaucracies that have never treated a single patient—including Anthony Fauci, Bill Gates, EcoHealth Alliance, the CDC, WHO, state public health officers and hospital administrators.[23,38]

The media (TV, newspapers, magazines, etc), medical societies, state medical boards and the owners of social media have appointed themselves to be the sole source of information concerning this so-called "pandemic". Websites have been removed, highly credentialed and experienced clinical doctors and scientific experts in the field of infectious diseases have been demonized, careers have been destroyed and all dissenting information has been labeled "misinformation" and "dangerous lies", even when sourced from top experts in the fields of virology, infectious diseases, pulmonary critical care, and epidemiology. These blackouts of truth occur even when this information is backed by extensive scientific citations from some of the most qualified medical specialists in the world.[23] Incredibly, even individuals, such as Dr. Michael Yeadon, a retired ex-Chief Scientist, and vice-president for the science division of Pfizer Pharmaceutical company in the UK, who charged the company with making an extremely dangerous vaccine, is ignored and demonized. Further, he, along with other highly qualified scientists have stated that no one should take this vaccine.

Dr. Peter McCullough, one of the most cited experts in his field, who has successfully treated over 2000 COVID patients by using a protocol of early treatment (which the so-called experts completely ignored), has been the victim of a particularly vicious assault by those benefiting financially from the vaccines. He has published his results in peer reviewed journals, reporting an 80% reduction in hospitalizations and a 75% reduction in deaths by using early treatment.

[44] Despite this, he is under an unrelenting series of attacks by the information controllers, none of which have treated a single patient.

Neither Anthony Fauci, the CDC, WHO nor any medical governmental establishment has ever offered any early treatment other than Tylenol, hydration and call an ambulance once you have difficulty breathing. This is unprecedented in the entire history of medical care as early treatment of infections is critical to saving lives and preventing severe complications. Not only have these medical organizations and federal lapdogs not even suggested early treatment, they attacked anyone who attempted to initiate such treatment with all the weapons at their disposal—loss of license, removal of hospital privileges, shaming, destruction of reputations and even arrest.[2]

A good example of this outrage against freedom of speech and providing informed consent information is the recent suspension by the medical board in Maine of Dr. Meryl Nass' medical license and the ordering of her to undergo a psychiatric evaluation for prescribing Ivermectin and sharing her expertise in this field.[9,65] I know Dr, Nass personally and can vouch for her integrity, brilliance and dedication to truth. Her scientific credentials are impeccable. This behavior by a medical licensing board is reminiscent of the methodology of the Soviet KGB during the period when dissidents were incarcerated in psychiatric gulags to silence their dissent.

OTHER UNPRECEDENTED ATTACKS

Another unprecedented tactic is to remove dissenting doctors from their positions as journal editors, reviewers and retracting of their scientific papers from journals, even after these papers have been in print. Until this pandemic event, I have never seen so many journal papers being retracted—the vast majority promoting alternatives to official dogma, especially if the papers question vaccine safety. Normally a submitted paper or study is reviewed by experts in the field, called peer review. These reviews can be quite intense and nit picking in detail, insisting that all errors within the paper be corrected before publication. So, unless fraud or some other major hidden problem is discovered after the paper is in print, the paper remains in the scientific literature.

We are now witnessing a growing number of excellent scientific papers, written by top experts in the field, being retracted from major medical and scientific journals weeks, months and even years after publication. A careful review indicates that in far too many instances the authors dared question accepted dogma by the controllers of scientific publications—especially concerning the safety, alternative treatments or efficacy of vaccines.[12,63] These journals rely on extensive adverting by pharmaceutical companies for their revenue. Several instances have occurred where powerful pharmaceutical companies exerted their influence on owners of these journals to remove articles that in any way question these companies' products.[13,34,35]

Worse still is the actual designing of medical articles for promoting drugs and pharmaceutical products that involve fake studies, so-called ghostwritten articles.[49,64] Richard Horton is quoted by the Guardian as saying "journals have devolved into information laundering operations for the pharmaceutical industry."[13,63] Proven fraudulent "ghostwritten" articles sponsored by pharmaceutical giants have appeared regularly in top clinical journals, such as JAMA, and New England Journal of Medicine—never to be removed despite proven scientific abuse and manipulation of data.[49,63]

Ghostwritten articles involve using planning companies whose job it is to design articles containing manipulated data to support a pharmaceutical product and then have these articles accepted by high-impact clinical journals, that is, the journals most likely to affect clinical decision making of doctors. Further, they supply doctors in clinical practice with free reprints of these manipulated articles. The Guardian found 250 companies engaged in this ghostwriting business. The final step in designing these articles for publication in the most prestigious journals is to recruit well recognized medical experts from prestigious institutions, to add their name to these articles. These recruited medical authors are either paid upon agreeing to add their name to these pre-written articles or they do so for the prestige of having their name on an article in a prestigious medical journal.[11]

Of vital importance is the observation by experts in the field of medical publishing that nothing has been done to stop this abuse. Medical ethicists have lamented that because of this widespread practice "you can't trust anything." While some journals insist on disclosure information, most doctors reading these articles ignore this information or excuse it and several journals make disclosure more difficult by requiring the reader to find the disclosure statements at another location. Many journals do not police such statements and omissions by authors are common and without punishment.

As concerns the information made available to the public, virtually all the media is under the control of these pharmaceutical giants or others who are benefitting from this "pandemic". Their stories are all the same, both in content and even wording. Orchestrated coverups occur daily and massive data exposing the lies being generated by these information controllers are hidden from the public. All data coming over the national media (TV, newspaper and magazines), as well as the local news you watch every day, comes only from "official" sources—most of which are lies, distortions or completely manufactured out of whole cloth—all aimed to deceive the public.

Television media receives the majority of its advertising budget from the international pharmaceutical companies—this creates an irresistible influence to report all concocted studies supporting their vaccines and other so-called treatments.[14] In 2020 alone the pharmaceutical industries spent 6.56 billion dollars on such advertising.[13,14] Pharma TV advertising amounted to 4.58 billion, an incredible 75% of their budget. That buys a lot of influence and control over the media. World famous experts within all fields of infectious diseases are excluded from media exposure and from social media should they in any way deviate against the concocted lies and distortions by the makers of these vaccines. In addition, these pharmaceutical companies spend tens of millions on social media advertising, with Pfizer leading the pack with $55 million in 2020.[14]

While these attacks on free speech are terrifying enough, even worse is the virtually universal control hospital administrators have exercised over the details of medical care in hospitals. These hirelings are now instructing doctors which treatment protocols they will adhere to and which treatments they will not use, no matter how harmful the "approved" treatments are or how beneficial the "unapproved" treatments are.[33,57]

Never in the history of American medicine have hospital administrators dictated to its physicians how they will practice medicine and what medications they can use. The CDC has no authority to dictate to hospitals or doctors concerning medical treatments. Yet, most physicians complied without the slightest resistance.

The federal Care Act encouraged this human disaster by offering all US hospitals up to 39,000 dollars for each ICU patient they put on respirators, despite the fact that early on it was obvious that the respirators were a major cause of death among these unsuspecting, trusting patients. In addition, the hospitals received 12,000 dollars for each patient that was admitted to the ICU—explaining, in my opinion and others, why all federal medical bureaucracies (CDC, FDA, NIAID, NIH, etc) did all in their power to prevent life-saving early treatments.[46] Letting patients deteriorate to the point they needed hospitalization, meant big money for all hospitals. A growing number of hospitals are in danger of bankruptcy, and many have closed their doors, even before this "pandemic".[50] Most of these hospitals are now owned by national or international corporations, including teaching hospitals.[10]

It is also interesting to note that with the arrival of this "pandemic" we have witnessed a surge in hospital corporate chains buying up a number of these financially at-risk hospitals.[1,54] It has been noted that billions in Federal Covid aid is being used by these hospital giants to acquire these financially endangered hospitals, further increasing the power of corporate medicine over physician independence. Physicians expelled from their hospitals are finding it difficult to find other hospitals staffs to join since they too may be owned by the same corporate giant. As a result, vaccine mandate policies include far larger numbers of hospital employees. For example, Mayo Clinic fired 700 employees for exercising their right to refuse a dangerous, essentially untested experimental vaccine.[51,57] Mayo Clinic did this despite the fact that many of these employees worked during the worst of the epidemic and are being fired when the Omicron variant is the dominant strain of the virus, has the pathogenicity of a common cold for most and the vaccines are ineffective in preventing the infection.

In addition, it has been proven that the vaccinated asymptomatic person has a nasopharyngeal titer of the virus as high as an infected unvaccinated person. If the purpose of the vaccine mandate is to prevent viral spread among the hospital staff and patients, then it is the vaccinated who present the greatest risk of transmission, not the unvaccinated. The difference is that a sick unvaccinated person would not go to work, the asymptomatic vaccinated spreader will.

What we do know is that major medical centers, such as Mayo Clinic, receive tens of millions of dollars in NIH grants each year as well as monies from the pharmaceutical makers of these experimental "vaccines". In my view, that is the real consideration driving these policies. If this could be proven in a court of law the administrators making these mandates should be prosecuted to the fullest extent of the law and sued by all injured parties.

The hospital bankruptcy problem has grown increasingly acute due to hospitals vaccine mandates and resulting large number of hospitals staff, especially nurses, refusing to be forcibly vaccinated.[17,51] This is all unprecedented in the history of medical care. Doctors within hospitals are responsible for the treatment of their individual patients and work directly with these patients and their families to initiate these treatments. Outside organizations, such as the CDC, have no authority to intervene in these treatments and to do so exposes the patients to grave errors by an organization that has never treated a single COVID-19 patient.

When this pandemic started, hospitals were ordered by the CDC to follow a treatment protocol that resulted in the deaths of hundreds of thousands of patients, most of whom would have recovered had proper treatments been allowed.[43,44] The majority of these deaths could have been prevented had doctors been allowed to use early treatment with such products as Ivermectin, hydroxy-chloroquine and a number of other safe drugs and natural compounds. It has been estimated, based on results by physicians treating the most covid patients successfully, that of the 800,000 people that we are told died from Covid, 640,000 could have not only been saved, but could have, in many cases, returned to their pre-infection health status had mandated early treatment

with these proven methods been used. This neglect of early treatment constitutes mass murder. That means 160,000 would have actually died, far less than the number dying at the hands of bureaucracies, medical associations and medical boards that refused to stand up for their patients. According to studies of early treatment of thousands of patients by brave, caring doctors, seventy-five to eighty percent of the deaths could have been prevented.[43,44]

Incredibly, these knowledgeable doctors were prevented from saving these Covid-19 infected people. It should be an embarrassment to the medical profession that so many doctors mindlessly followed the deadly protocols established by the controllers of medicine.

One must also keep in mind that this event never satisfied the criteria for a pandemic. The World Health Organization changed the criteria to make this a pandemic. To qualify for a pandemic status the virus must have a high mortality rate for the vast majority of people, which it didn't (with a 99.98% survival rate), and it must have no known existing treatments—which this virus had—in fact, a growing number of very successful treatments.

The draconian measures established to contain this contrived "pandemic" have never been shown to be successful, such as masking the public, lockdowns, and social distancing. A number of carefully done studies during previous flu seasons demonstrated that masks, of any kind, had never prevented the spread of the virus among the public.[60]

In fact, some very good studies suggested that the masks actually spread the virus by giving people a false sense of security and other factors, such as the observation that people were constantly breaking sterile technique by touching their mask, improper removal and by leakage of infectious aerosols around the edges of the mask. In addition masks were being disposed of in parking lots, walking trails, laid on tabletops in restaurants and placed in pockets and purses.

Within a few minutes of putting on the mask, a number of pathogenic bacteria can be cultured from the masks, putting the immune suppressed person at a high risk of bacterial pneumonia and children at a higher risk of meningitis.[16] A study by researchers at the University of Florida cultured over 11 pathogenic bacteria from the inside of the mask worn by children in schools.[40]

It was also known that children were at essentially no risk of either getting sick from the virus or transmitting it.

In addition, it was also known that wearing a mask for over 4 hours (as occurs in all schools) results in significant hypoxia (low blood oxygen levels) and hypercapnia (high CO2 levels), which have a number of deleterious effects on health, including impairing the development of the child's brain.[4,72,52]

We have known that brain development continues long after the grade school years. A recent study found that children born during the "pandemic" have significantly lower IQs—yet school boards, school principals and other educational bureaucrats are obviously unconcerned.[18]

TOOLS OF THE INDOCTRINATION TRADE

The designers of this pandemic anticipated a pushback by the public and that major embarrassing questions would be asked. To prevent this, the controllers fed the media a number of tactics, one of the most commonly used was and is the "fact check" scam. With each confrontation with carefully documented evidence, the media "fact checkers" countered with the charge of "misinformation", and an unfounded "conspiracy theory" charge that was, in their lexicon, "debunked". Never were we told who the fact checkers were or the source of their "debunking" information—we were just to believe the "fact checkers". A recent court case established under oath that facebook "fact checkers" used their own staff opinion and not real experts to check "facts".[59] When sources are in fact revealed they are invariably the corrupt CDC, WHO or Anthony Fauci or just their opinion. Here is a list of things that were labeled as "myths" and "misinformation" that were later proven to be true.

- The asymptomatic vaccinated are spreading the virus equally as with unvaccinated symptomatic infected.
- The vaccines cannot protect adequately against new variants, such as Delta and Omicron.
- Natural immunity is far superior to vaccine immunity and is most likely lifelong.
- Vaccine immunity not only wanes after several months, but all immune cells are impaired for prolonged periods, putting the vaccinated at a high risk of all infections and cancer.
- COVID vaccines can cause a significant incidence of blood clots and other serious side effects
- The vaccine proponents will demand numerous boosters as each variant appears on the scene.
- Fauci will insist on the covid vaccine for small children and even babies.
- Vaccine passports will be required to enter a business, fly in a plane, and use public transportation
- There will be internment camps for the unvaccinated (as in Australia, Austria and Canada)
- The unvaccinated will be denied employment.
- There are secret agreements between the government, elitist institutions, and vaccine makers
- Many hospitals were either empty or had low occupancy during the pandemic.
- The spike protein from the vaccine enters the nucleus of the cell, altering cell DNA repair function.
- Hundreds of thousands have been killed by the vaccines and many times more have been permanently damaged.

- Early treatment could have saved the lives of most of the 700,000 who died.
- Vaccine-induced myocarditis (which was denied initially) is a significant problem and clears over a short period.
- Special deadly lots (batches) of these vaccines are mixed with the mass of other Covid-19 vaccines

Several of these claims by those opposing these vaccines now appear on the CDC website—most still identified as "myths". Today, extensive evidence has confirmed that each of these so-called "myths" were in fact true. Many are even admitted by the "saint of vaccines", Anthony Fauci. For example, we were told, even by our cognitively impaired President, that once the vaccine was released all the vaccinated people could take off their masks. Oops! We were told shortly afterward—the vaccinated have high concentrations (titers) of the virus in their noses and mouths (nasopharynx) and can transmit the virus to others in which they come into contact—especially their own family members. On go the masks once again—in fact double masking is recommended. The vaccinated are now known to be the main superspreaders of the virus and hospitals are filled with the sick vaccinated and people suffering from serious vaccine complications.[27,42,45]

Another tactic by the vaccine proponents is to demonize those who reject being vaccinated for a variety of reasons. The media refers to these critically thinking individuals as "anti-vaxxers", "vaccine deniers", "Vaccine resisters", "murders", "enemies of the greater good" and as being the ones prolonging the pandemic. I have been appalled by the vicious, often heartless attacks by some of the people on social media when a parent or loved one relates a story of the terrible suffering and eventual death, they or their loved one suffered as a result of the vaccines. Some psychopaths tweet that they are glad that the loved one died or that the dead vaccinated person was an enemy of good for telling of the event and should be banned. This is hard to conceptualize. This level of cruelty is terrifying, and signifies the collapse of a moral, decent, and compassionate society.

It is bad enough for the public to sink this low, but the media, political leaders, hospital administrators, medical associations and medical licensing boards are acting in a similar morally dysfunctional and cruel way.

LOGIC, REASONING, AND SCIENTIFIC EVIDENCE HAS DISAPPEARED IN THIS EVENT

Has scientific evidence, carefully done studies, clinical experience and medical logic had any effect on stopping these ineffective and dangerous vaccines? Absolutely not! The draconian efforts to vaccinate everyone on the planet continues (except the elite, postal workers, members of Congress and other insiders).[31,62]

In the case of all other drugs and previous conventional vaccines under review by the FDA, the otherwise unexplained deaths of 50 or less individuals would result in a halt in further distribution of the product, as happened on 1976 with the swine flu vaccine. With over 18,000 deaths being reported by the VAERS system for the period December 14, 2020 and December 31st, 2021 as well as 139,126 serious injuries (including deaths) for the same period there is still no interest in stopping this deadly vaccine program.[61] Worse, there is no serious investigation by any government agency to determine why these people are dying and being seriously and permanently injured by these vaccines.[15,67] What we do see is a continuous series of coverups and evasions by the vaccine makers and their promoters.

The war against effective cheap and very safe repurposed drugs and natural compounds, that have proven beyond all doubt to have saved millions of lives all over the world, has not only continued but has stepped up in intensity.[32,34,43]

Doctors are told they cannot provide these life-saving compounds for their patients and if they do, they will be removed from the hospital, have their medical license removed or be punished in many other ways. A great many pharmacies have refused to fill prescriptions for lvermectin or hydroxy-chloroquine, despite the fact that millions of people have taken these drugs safely for over 60 years in the case of hydroxy chloroquine and decades for Ivermectin.[33,36] This refusal to fill prescriptions is unprecedented and has been engineered by those wanting to prevent alternative methods of treatment, all based on protecting vaccine expansion to all. Several companies that make hydroxy chloroquine agreed to empty their stocks of the drug by donating them to the Strategic National Stockpile, making this drug far more difficult to get.[33] Why would the government do that when over 30 well-done studies have shown that this drug reduced deaths anywhere from 66% to 92% in other countries, such as India, Egypt, Argentina, France, Nigeria, Spain, Peru, Mexico, and others?[23]

The critics of these two life-saving drugs are most often funded by Bill Gates and Anthony Fauci, both of which are making millions from these vaccines.[48,15]

To further stop the use of these drugs, the pharmaceutical industry and Bill Gates/Anthony Fauci funded fake research to make the case that hydroxy chloroquine was a dangerous drug and could damage the heart.[34] To make this fraudulent case the researchers administered the sickest of covid patients a near lethal dose of the drug, in a dose far higher than used on any covid patient by Dr. Kory, McCullough and other "real", and compassionate doctors, physicians who were actually treating covid patients.[23]

The controlled, lap-dog media, of course, hammered the public with stories of the deadly effect of hydroxy-chloroquine, all with a terrified look of fake panic. All these

stories of ivermectin dangers were shown to be untrue and some of the stories were incredibly preposterous.[37,43]

The attack on Ivermectin was even more vicious than against hydroxy-chloroquine. All of this, and a great deal more is meticulously chronicled in Robert Kennedy, Jr's excellent new book—*The Real Anthony Fauci. Bill Gates, Big Pharma, and the Global War on Democracy and Public Health*.[32] If you are truly concerned with the truth and with all that has occurred since this atrocity started, you must not only read, but study this book carefully. It is fully referenced and covers all topics in great detail. This is a designed human tragedy of Biblical proportions by some of the most vile, heartless, psychopaths in history.

Millions have been deliberately killed and crippled, not only by this engineered virus, but by the vaccine itself and by the draconian measures used by these governments to "control the pandemic spread". We must not ignore the "deaths by despair" caused by these draconian measures, which can exceed hundreds of thousands. Millions have starved in third world countries as a result. In the United States alone, of the 800,000 who died, claimed by the medical bureaucracies, well over 600,000 of these deaths were the result of the purposeful neglect of early treatment, blocking the use of highly effective and safe repurposed drugs, such as hydroxy-chloroquine and Ivermectin, and the forced use of deadly treatments such as remdesivir and use of ventilators. This does not count the deaths of despair and neglected medical care caused by the lockdown and hospital measures forced on healthcare systems.

To compound all this, because of vaccine mandates among all hospital personnel, thousands of nurses and other hospital workers have resigned or been fired.[17,30,51] This has resulted in critical shortages of these vital healthcare workers and dangerous reductions of ICU beds in many hospitals. In addition, as occurred in the Lewis County Healthcare System, a specialty-hospital system in Lowville, N.Y., closed its maternity unit following the resignation of 30 hospital staff over the state's disastrous vaccine mandate orders. The irony in all these cases of resignations is that the administrators unhesitatingly accepted these mass staffing losses despite rantings about suffering from short staffing during a "crisis". This is especially puzzling when we learned that the vaccines did not prevent viral transmission and the present predominant variant is of extremely low pathogenicity.

DANGERS OF THE VACCINES ARE INCREASINGLY REVEALED BY SCIENCE

While most researchers, virologists, infectious disease researchers and epidemiologists have been intimidated into silence, a growing number of high integrity individuals with tremendous expertise have come forward to tell the truth—that is, that these vaccines are deadly.

Most new vaccines must go through extensive safety testing for years before they are approved. New technologies, such as the mRNA and DNA vaccines, require a minimum of 10 years of careful testing and extensive follow-up. These new so-called vaccines were "tested" for only 2 months and then the results of these safety test were and continue to be kept secret. Testimony before Senator Ron Johnson by several who participated in the 2 months study indicates that virtually no follow-up of the participants of the pre-release study was ever done.[67] Complains of complications were ignored and despite promises by Pfizer that all medical expenses caused by the "vaccines" would be paid by Pfizer, these individuals stated that none were paid.[66] Some medical expenses exceed 100,000 dollars.

As an example of the deception by Pfizer, and the other makers of mRNA vaccines, is the case of 12-year-old Maddie de Garay, who participated in the Pfizer vaccine pre-release safety study. At Sen. Johnson's presentation with the families of the vaccine injured, her mother told of her child's recurrent seizures, that she is now confined to a wheelchair, must be tube fed and suffers permanent brain damage. On the Pfizer safety evaluation submitted to the FDA her only side effect is listed as having a "stomachache". Each person submitted similar horrifying stories.

The Japanese resorted to a FOIA (Freedom of Information Act) lawsuit to force Pfizer to release its secret biodistribution study. The reason Pfizer wanted it kept secret is that it demonstrated that Pfizer lied to the public and the regulatory agencies about the fate of the injected vaccine contents (the mRNA enclosed nano-lipid carrier). They claimed that it remained at the site of the injection (the shoulder), when in fact their own study found that it rapidly spread throughout the entire body by the bloodstream within 48 hours.

The study also found that these deadly nano-lipid carriers collected in very high concentrations in several organs, including the reproductive organs of males and females, the heart, the liver, the bone marrow, and the spleen (a major immune organ). The highest concentration was in the ovaries and the bone marrow. These nano-lipid carriers also were deposited in the brain.

Dr. Ryan Cole, a pathologist from Idaho reported a dramatic spike in highly aggressive cancers among vaccinated individuals, (not reported in the Media). He found a frighteningly high incidence of highly aggressive cancers in vaccinated individuals, especially highly invasive melanomas in young people and uterine cancers in women.[26] Other reports of activation of previously controlled cancers are also appearing among vaccinated cancer patients.[47] Thus far, no studies have been done to confirm these reports, but it is unlikely such studies will be done, at least studies funded by grants from the NIH.

The high concentration of spike proteins found in the ovaries in the biodistribution study could very well impair fertility in young women, alter menstruation, and could put them at an increased risk of ovarian cancer. The high concentration in the bone marrow, could also put the vaccinated at a high risk of leukemia and lymphoma. The leukemia risk is very worrisome now that they have started vaccinating children as young as 5 years of age. No long-term studies have been conducted by any of these makers of Covid-19 vaccines, especially as regards the risk of cancer induction. Chronic inflammation is intimately linked to cancer induction, growth and invasion and vaccines stimulate inflammation.

Cancer patients are being told they should get vaccinated with these deadly vaccines. This, in my opinion, is insane. Newer studies have shown that this type of vaccine inserts the spike protein within the nucleus of the immune cells (and most likely many cell types) and once there, inhibits two very important DNA repair enzymes, BRCA1 and 53BP1, whose duty it is to repair damage to the cell's DNA.[29] Unrepaired DNA damage plays a major role in cancer.

There is a hereditary disease called xeroderma pigmentosum in which the DNA repair enzymes are defective. These ill-fated individuals develop multiple skin cancers and a very high incidence of organ cancer as a result. Here we have a vaccine that does the same thing, but to a less extensive degree.

One of the defective repair enzymes caused by these vaccines is called BRCA1, which is associated with a significantly higher incidence of breast cancer in women and prostate cancer in men.

It should be noted that no studies were ever done on several critical aspects of this type of vaccine.

- They have never been tested for long term effects
- They have never been tested for induction of autoimmunity
- They have never been properly tested for safety during any stage of pregnancy
- No follow-up studies have been done on the babies of vaccinated women
- There are no long-term studies on the children of vaccinated pregnant women after their birth (Especially as neurodevelopmental milestone occur).
- It has never been tested for effects on a long list of medical conditions:
  - Diabetes
  - Heart disease
  - Atherosclerosis
  - Neurodegenerative diseases
  - Neuropsychiatric effects
  - Induction of autism spectrum disorders and schizophrenia
  - Long term immune function
  - Vertical transmission of defects and disorders
  - Cancer
  - Autoimmune disorders

Previous experience with the flu vaccines clearly demonstrates that the safety studies done by researchers and clinical doctors with ties to pharmaceutical companies were essentially all either poorly done or purposefully designed to falsely show safety and coverup side effects and complications. This was dramatically demonstrated with the previously mentioned phony studies designed to indicate that hydroxy Chloroquine and Ivermectin were ineffective and too dangerous to use.[34,36,37] These fake studies resulted in millions of deaths and severe health disasters worldwide. As stated, 80% of all deaths were unnecessary and could have been prevented with inexpensive, safe repurposed medications with a very long safety history among millions who have taken them for decades or even a lifetime.[43,44]

It is beyond ironic that those claiming that they are responsible for protecting our health approved a poorly tested set of vaccines that has resulted in more deaths in less than a year of use than all the other vaccines combined given over the past 30 years. Their excuse when confronted was—"we had to overlook some safety measures because this was a deadly pandemic".[28,46]

In 1986 President Reagan signed the National Childhood Vaccine Injury Act, which gave blanket protection to pharmaceutical makers of vaccines against injury litigation by families of vaccine injured individuals. The Supreme Court, in a 57-page opinion, ruled in favor of the vaccine companies, effectively allowing vaccine makers to manufacture and distribute dangerous, often ineffective vaccines to the population without fear of legal consequences. The court did insist on a vaccine injury compensation system which has paid out only a very small number of rewards to a large number of severely injured individuals. It is known that it is very difficult to receive these awards. According to the Health Resources and Services Administration, since 1988 the Vaccine Injury Compensation Program (VICP) has agreed to pay 3,597 awards among 19,098 vaccine injured individuals applying amounting to a total sum of $3.8 billion. This was prior to the introduction of the Covid-19 vaccines, in which the deaths alone exceed all deaths related to all the vaccines combined over a thirty-year period.

In 2018 President Trump signed into law the "right-to-try" law which allowed the use of experimental drugs and all unconventional treatments to be used in cases of extreme medical conditions. As we have seen with the refusal of many hospitals and even blanket refusal by states to allow Ivermectin, hydroxy-chloroquine or any other unapproved "official" methods to treat even terminal Covid-19 cases, these nefarious individuals have ignored this law.

Strangely, they did not use this same logic or the law when it came to Ivermectin and Hydroxy Chloroquine, both of which had undergone extensive safety testing by over 30 clinical studies of a high quality and given glowing reports on both efficacy and safety in numerous countries. In addition, we had a record of use for up to 60 years by millions of people, using these drugs worldwide, with an excellent safety record. It was obvious that a group of very powerful people in conjunction with pharmaceutical conglomerates didn't want the pandemic to end and wanted vaccines as the only treatment option. Kennedy's book makes this case using extensive evidence and citations.[14,32]

Dr. James Thorpe, an expert in maternal-fetal medicine, demonstrates that these covoid-19 vaccines given during pregnancy have resulted in a 50-fold higher incidence of miscarriage than reported with all other vaccines combined.[28] When we examine his graph on fetal malformations there was a 144-fold higher incidence of fetal malformation with the Covid-19 vaccines given during pregnancy as compared to all other vaccines combined. Yet, the American Academy of Obstetrics and Gynecology and the American College of Obstetrics and Gynecology endorse the safety of these vaccines for all stages of pregnancy and among women breast feeding their babies.

It is noteworthy that these medical specialty groups have received significant funding from Pfizer pharmaceutical company. The American College of Obstetrics and Gynecology, just in the 4th quarter of 2010, received a total of $11,000 from Pfizer Pharmaceutical company alone.[70] Funding from NIH grants are much higher.[20] The best way to lose these grants is to criticize the source of the funds, their products or pet programs. Peter Duesberg, because of his daring to question Fauci's pet theory of AIDS caused by HIV virus, was no longer awarded any of the 30 grant applications he submitted after going public. Prior to this episode, as the leading authority on retroviruses in the world, he had never been turned down for an NIH grant.[39] This is how the "corrupted" system works, even though much of the grant money comes from our taxes.

HOT LOTS—DEADLY BATCHES OF THE VACCINES

A new study has now surfaced, the results of which are terrifying.[25] A researcher at Kingston University in London, has completed an extensive analysis of the VAERs data (a subdepartment of the CDC which collects voluntary vaccine complication data), in which he grouped reported deaths following the vaccines according to the manufacturer's lot numbers of the vaccines. Vaccines are manufactured in large batches called lots. What he discovered was that the vaccines are divided into over 20,000 lots and that one out of every 200 of these batches (lots) is demonstrably deadly to anyone who receives a vaccine from that lot, which includes thousands of vaccine doses.

He examined all manufactured vaccines—Pfizer, Moderna, Johnson and Johnson (Janssen), etc. He found that among every 200 batches of the vaccine from Pfizer and other makers, one batch of the 200 was found to be over 50x more deadly than vaccines batches from other lots. The other vaccine lots (batches) were also causing deaths and disabilities, but nowhere near to this extent. These deadly batches should have appeared randomly among all "vaccines" if it was an unintentional event. However, he found that 5% of the vaccines were responsible for 90% of the serious adverse events, including deaths. The incidence of deaths and serious complications among these "hot lots" varied from over 1000% to several thousand percent higher than comparable safer lots. If you think this was by accident—think again. This is not the first time "hot lots" were, in my opinion, purposefully manufactured and sent across the nation—usually vaccines designed for children. In one such scandal, "hot lots" of a vaccine ended up all in one state and the damage immediately became evident. What was the manufacture's response? It wasn't to remove the deadly batches of the vaccine. He ordered his company to scatter the hot lots across the nation so that authorities would not see the obvious deadly effect.

All lots of a vaccine are numbered—for example Modera labels them with such codes as 013M20A. It was noted that the batch numbers ended in either 20A or 21A. Batches ending in 20A were much more toxic than the ones ending in 21A. The batches ending in 20A had about 1700 adverse events, versus a few hundred to twenty or thirty events for the 21A batches. This example explains why some people had few or no adverse events after taking the vaccine while others are either killed or severely and permanently harmed. To see the researcher's explanation, go to https://www.bitchute.com/video/6xIYPZBkydsu/ In my opinion these examples strongly suggest an intentional alteration of the production of the "vaccine" to include deadly batches.

I have met and worked with a number of people concerned with vaccine safety and I can tell you they are not the evil anti-vaxxers you are told they are. They are highly principled, moral, compassionate people, many of which are top researchers and people who have studied the issue extensively. Robert Kennedy, Jr, Barbara Lou Fisher, Dr. Meryl Nass, Professor Christopher Shaw, Megan Redshaw, Dr. Sherri Tenpenny, Dr. Joseph Mercola, Neil Z. Miller, Dr. Lucija Tomjinovic, Dr. Stephanie Seneff, Dr. Steve Kirsch and Dr. Peter McCullough just to name a few. These people have nothing to gain and a lot to lose. They are attacked viciously by the media, government agencies, and elite billionaires who think they should control the world and everyone in it.

WHY DID FAUCI WANT NO AUTOPSIES OF THOSE WHO DIED AFTER VACCINATION?

There are many things about this "pandemic" that are unprecedented in medical history. One of the most startling is that at the height of the pandemic so few autopsies, especially total autopsies, were being done. A mysterious virus was rapidly spreading around the world, a selected group of people with weakened immune systems were getting seriously ill and many were dying and the one way we could rapidly gain the most knowledge about this virus—an autopsy, was being discouraged.

Guerriero noted that by the end of April, 2020 approximately 150,000 people had died, yet there were only 16 autopsies performed and reported in the medical literature.[24] Among these, only seven were complete autopsies, the remaining 9 being partial or by needle biopsy or incisional biopsy. Only after 170,000 deaths by Covid-19 and four months into the pandemic were the first series of autopsies actually done, that is, more than ten. And only after 280,000 deaths and another month, were the first large series of autopsies performed, some 80 in number.[22] Sperhake, in a call for autopsies to be done without question, noted that the first full autopsy reported in the literature along with photomicrographs appeared in a medico-legal journal from China in February 2020.[41,68] Sperhake expressed confusion as to why there was a reluctance to perform autopsies during the crisis, but he knew it was not coming from the pathologists. The medical literature was littered with appeals by pathologist for more autopsies to be performed.[58] Sperhake further noted that the Robert Koch Institute (The German health monitoring system) at least initially advised against doing autopsies. He also knew that at the time 200 participating autopsy institutions in the United States had done at least 225 autopsies among 14 states.

Some have claimed that this dearth of autopsies was based on the government's fear of infection among the pathologists, but a study of 225 autopsies on Covid-19 cases demonstrated only one case of infection among the pathologist and this was concluded to have been an infection contracted elsewhere.[19] Guerriero ends his article calling for more autopsies with this observation: "Shoulder to shoulder, clinical and forensic pathologists overcame the obstructions of autopsy studies in Covid-19 victims and hereby generated valuable knowledge on the pathophysiology of the interaction between the SARS-CoV-2 and the human body, thus contributing to our understanding of the disease."[24]

Suspicion concerning the worldwide reluctance of nations to allow full post mortem studies of Covid-19 victims may be based on the idea that it was more than by chance. There are at least two possibilities that stand out. First, those leading the progression of this "non-pandemic" event into a perceived worldwide "deadly pandemic", were hiding an important secret that autopsies could document. Namely, just how many of the deaths were actually caused by the virus? To implement draconian measures, such as mandated mask wearing, lockdowns, destruction of businesses, and eventually mandated forced vaccination, they needed very large numbers of covid-19 infected dead. Fear would be the driving force for all these destructive pandemic control programs.

Elder et al in his study classified the autopsy findings into four groups.[22]

1. Certain Covid-19 death
2. Probably Covid-19 death
3. Possible Covid-19 death
4. Not associated with Covid-19, despite the positive test.

What possibly concerned or even terrified the engineers of this pandemic was that autopsies just might, and did, show that a number of these so-called Covid-19 deaths in truth died of their comorbid diseases. In the vast majority of autopsy studies reported, pathologists noted multiple comorbid conditions, most of which at the extremes of life could alone be fatal. Previously it was known that common cold viruses had an 8% mortality in nursing homes.

In addition, valuable evidence could be obtained from the autopsies that would improve clinical treatments and could possibly demonstrate the deadly effect of the CDC mandated protocols all hospitals were required to follow, such as the use of respirators and the deadly, kidney-destroying drug remdesivir. The autopsies also demonstrated accumulating medical errors and poor-quality care, as the shielding of doctors in intensive care units from the eyes of family members inevitably leads to poorer quality care as reported by several nurses working in these areas.[53-55]

As bad as all this was, the very same thing is being done in the case of Covid vaccine deaths—very few complete autopsies have been done to understand why these people died, that is, until recently. Two highly qualified researchers, Dr. Sucharit Bhakdi a microbiologist and highly qualified expert in infectious disease and Dr. Arne Burkhardt, a pathologist who is a widely published authority having been a professor of pathology at several prestigious institutions, recently performed autopsies on 15 people having died after vaccination. What they found explains why so many are dying and experiencing organ damage and deadly blood clots.[5]

They determined that 14 of the fifteen people died as a result of the vaccines and not of other causes. Dr. Burkhardt, the pathologist, observed widespread evidence of an immune attack on the autopsied individuals' organs and tissues—especially their heart. This evidence included extensive invasion of small blood vessels with massive numbers of lymphocytes, which cause extensive cell destruction when

unleashed. Other organs, such as the lungs and liver, were observed to have extensive damage as well. These findings indicate the vaccines were causing the body to attack itself with deadly consequences. One can easily see why Anthony Fauci, as well as public health officers and all who are heavily promoting these vaccines, publicly discouraged autopsies on the vaccinated who subsequently died. One can also see that in the case of vaccines, that were essentially untested prior to being approved for the general public, at least the regulatory agencies should have been required to carefully monitor and analyze all serious complications, and certainly deaths, linked to these vaccines. The best way to do that is with complete autopsies.

While we learned important information from these autopsies what is really needed are special studies of the tissues of those who have died after vaccination for the presence of spike protein infiltration throughout the organs and tissues. This would be critical information, as such infiltration would result in severe damage to all tissues and organs involved—especially the heart, the brain, and the immune system. Animal studies have demonstrated this. In these vaccinated individuals the source of these spike proteins would be the injected nanolipid carriers of the spike protein producing mRNA. It is obvious that the government health authorities and pharmaceutical manufacturers of these "vaccines" do not want these critical studies done as the public would be outraged and demand an end to the vaccination program and prosecution of the involved individuals who covered this up.

CONCLUSIONS

We are all living through one of the most drastic changes in our culture, economic system, as well as political system in our nation's history as well as the rest of the world. We have been told that we will never return to "normal" and that a great reset has been designed to create a "new world order". This has all been outlined by Klaus Schwab, head of the World Economic Forum, in his book on the "Great Reset".[66] This book gives a great deal of insight as to the thinking of the utopians who are proud to claim this pandemic "crisis" as their way to usher in a new world. This new world order has been on the drawing boards of the elite manipulators for over a century.[73,74] In this paper I have concentrated on the devastating effects this has had on the medical care system in the United States, but also includes much of the Western world. In past papers I have discussed the slow erosion of traditional medical care in the United States and how this system has become increasingly bureaucratized and regimented.[7,8] This process was rapidly accelerating, but the appearance of this, in my opinion, manufactured "pandemic" has transformed our health care system over night.

As you have seen, an unprecedented series of events have taken place within this system. Hospital administrators, for example, assumed the position of medical dictators, ordering doctors to follow protocols derived not from those having extensive experience in treating this virus, but rather from a medical bureaucracy that has never treated a single COVID-19 patient. The mandated use of respirators on ICU Covid-19 patients, for example, was imposed in all medical systems and dissenting physicians were rapidly removed from their positions as caregivers, despite their demonstration of markedly improved treatment methods. Further, doctors were told to use the drug remdesivir despite its proven toxicity, lack of effectiveness and high complication rate. They were told to use drugs that impaired respiration and mask every patient, despite the patient's impaired breathing. In each case, those who refused to abuse their patients were removed from the hospital and even faced a loss of license—or worse.

For the first time in modern medical history, early medical treatment of these infected patients was ignored nationwide. Studies have shown that early medical treatment was saving 80% of higher number of these infected people when initiated by independent doctors.[43,44] Early treatment could have saved over 640,000 lives over the course of this "pandemic". Despite the demonstration of the power of these early treatments, the forces controlling medical care continued this destructive policy.

Families were not allowed to see their loved ones, forcing these very sick individuals in the hospitals to face their deaths alone. To add insult to injury, funerals were limited to a few grieving family members, who were not allowed to even sit together. All the while large stores, such as Walmart and Cosco were allowed to operate with minimal restrictions. Nursing home patients were also not allowed to have family visitations, again being forced to die a lonely death. All the while, in a number of states, the most transparent being in New York state, infected elderly were purposefully transferred from hospitals into nursing homes, resulting in a very high death rates of these nursing home residents. At the beginning of this "pandemic" over 50% of all death were occurring in nursing homes.

Throughout this "pandemic" we have been fed an unending series of lies, distortions and disinformation by the media, the public health officials, medical bureaucracies (CDC, FDA and WHO) and medical associations. Physicians, scientists, and experts in infectious treatments who formed associations designed to develop more effective and safer treatments, were regularly demonized, harassed, shamed, humiliated, and experience a loss of licensure, loss of hospital privileges and, in at least one case, ordered to have a psychiatric examination.[2,65,71]

Anthony Fauci was given essentially absolute control of all forms of medical care during this event, including insisting that drugs he profited from be used by all treating physicians. He ordered the use of masks, despite at first laughing at the

use of masks to filter a virus. Governors, mayors, and many businesses followed his orders without question.

The draconian measures being used, masking, lockdowns, testing of the uninfected, use of the inaccurate PCR test, social distancing, and contact tracing had been shown previously to be of little or no use during previous pandemics, yet all attempts to reject these methods were to no avail. Some states ignored these draconian orders and had either the same or fewer cases, as well as deaths, as the states with the most strictly enforced measures. Again, no amount of evidence or obvious demonstration along these lines had any effect on ending these socially destructive measures. Even when entire countries, such as Sweden, which avoided all these measures, demonstrated equal rates of infections and hospitalization as nations with the strictest, very draconian measures, no policy change by the controlling institutions occurred. No amount of evidence changed anything.

Experts in the psychology of destructive events, such as economic collapses, major disasters and previous pandemics demonstrated that draconian measures come with an enormous cost in the form of "deaths of despair" and in a dramatic increase in serious psychological disorders. The effects of these pandemic measures on children's neurodevelopment is catastrophic and to a large extent irreversible.

Over time tens of thousands could die as a result of this damage. Even when these predictions began to appear, the controllers of this "pandemic" continued full steam ahead. Drastic increases in suicides, a rise in obesity, a rise in drug and alcohol use, a worsening of many health measures and a terrifying rise in psychiatric disorders, especially depression and anxiety, were ignored by the officials controlling this event.

We eventually learned that many of the deaths were a result of medical neglect. Individuals with chronic medical conditions, diabetes, cancer, cardiovascular disease, and neurological diseases were no longer being followed properly in their clinics and doctor's offices. Non-emergency surgeries were put on hold. Many of these patients chose to die at home rather than risk going to the hospitals and many considered hospitals "death houses".

Records of deaths have shown that there was a rise in deaths among those aged 75 and older, mostly explained by Covid-19 infections, but for those between the ages of 65 to 74, deaths had been increasing well before the pandemic onset.[69] Between ages of 18 and aged 65 years, records demonstrate a shocking hike in non-Covid-19 deaths. Some of these deaths were explained by a dramatic increase in drug-related deaths, some 20,000 more than 2019. Alcohol related deaths also increased substantially, and homicides increased almost 30% in the 18 to 65-year group.

The head of the insurance company OneAmerica stated that their data indicated that the death rate for individuals aged 18 to 64 had increased 40% over the pre-pandemic period.[21] Scott Davidson, the company's CEO, stated that this represented the highest death rate in the history of insurance records, which does extensive data collections on death rates each year. Davidson also noted that this high of a death rate increase has never been seen in the history of death data collection. Previous catastrophes of monumental extent increased death rates no more than 10 percent, 40% is unprecedented.

Dr. Lindsay Weaver, Indiana's chief medical officer, stated that hospitalizations in Indiana are higher than at any point in the past five years. This is of critical importance since the vaccines were supposed to significantly reduce deaths, but the opposite has happened. Hospitals are being flooded with vaccine complications and people in critical condition from medical neglect caused by the lockdowns and other pandemic measures.[46,56]

A dramatic number of these people are now dying, with the spike occurring after the vaccines were introduced. The lies flowing from those who have appointed themselves as medical dictators are endless. First, we were told that the lockdown would last only two weeks, they lasted over a year. Then we were told that masks were ineffective and did not need to be worn. Quickly that was reversed. Then we were told the cloth mask was very effective, now it's not and everyone should be wearing an N95 mask and before that that they should double mask. We were told there was a severe shortage of respirators, then we discover they are sitting unused in warehouses and in city dumps, still in their packing crates. We were informed that the hospitals were filled mostly with the unvaccinated and later found the exact opposite was true the world over. We were told that the vaccine was 95% effective, only to learn that in fact the vaccines cause a progressive erosion of innate immunity.

Upon release of the vaccines, women were told the vaccines were safe during all states of pregnancy, only to find out no studies had been done on safety during pregnancy during the "safety tests" prior to release of the vaccine. We were told that careful testing on volunteers before the EUA approval for public use demonstrated extreme safety of the vaccines, only to learn that these unfortunate subjects were not followed, medical complications caused by the vaccines were not paid for and the media covered this all up.[67] We also learned that the pharmaceutical makers of the vaccines were told by the FDA that further animal testing was unnecessary (the general public would be the Guinea pigs.) Incredibly, we were told that the Pfizer's new mRNA vaccines had been approved by the FDA, which was a cleaver deception, in that another vaccine had approval (comirnaty) and not the one being used, the BioNTech vaccine. The approved comirnaty vaccine

was not available in the United States. The national media told the public that the Pfizer vaccine had been approved and was no longer classed as experimental, a blatant lie. These deadly lies continue. It is time to stop this insanity and bring these people to justice.

Disclaimer

The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Journal or its management.

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