We must halt all ongoing Covid-19 mass vaccination campaigns as a temporary health benefit to the most vulnerable groups does not justify *a public health disaster of international concern*.

Geert Vanden Bossche, DVM, PhD virology, independent seasoned vaccine researcher, previous SPO at the Bill & Melinda Gates Foundation and SPM at GAVI is urging WHO and world political leaders to immediately halt all ongoing Covid-19 mass vaccination campaigns as there is compelling evidence that they will soon dramatically worsen the consequences of the current pandemic.

Attached to this letter, you will find a *summary* of the manuscript I am currently in the process of finalizing. I initially intended to attach the manuscript in full to my letter. However, given the exceptional urgency of my call, I have no choice but to send you the summary (+ conclusion) in advance. I will post the manuscript in full on LinkedIn as soon as I can (presumably in the course of next week).

In the upcoming manuscript I will share my insights on the immune pathogenesis of Coronavirus pandemics. Those are based on an in-depth analysis of Covid-19-relevant scientific literature (key references will be appended) and backed by my deep vaccine knowledge and relentless perseverance in unraveling the host's immune defense mechanisms and strategies viruses have evolved to escape those. Understanding the interplay between the virus and the host immune system is a prerequisite for designing vaccines able to counter the immune subversive strategy of infectious pathogens. I do not think that it is reasonable for WHO or any other health authority to approve 'emergency use' of vaccines aimed at conducting mass vaccination campaigns in the very heat of an infectious pandemic without having gained an in-depth understanding of how this may impact on the outcome of the pandemic.

In particular, lack of understanding of the consequences of immune pressure on highly mutable viruses has now allowed for the approval of a number of Covid-19 vaccines that are completely contraindicated for fighting a pandemic, regardless of the technology used. ***Although safe and efficacious and providing temporary relief to part of the population and to healthcare facilities, these vaccines will soon come with a heavy toll to be paid by the entire population if mass vaccination campaigns continue.***

Again, given the urgency of my call, I will neither allow time for peer-review, nor for English proofreading, nor for fine-tuning the wording or for screening the manuscript for redundancy. As I merely seek to provide enough of compelling scientific proof for sounding this warning bell, I will not deal with relevant matters as exhaustively as I would normally do. Clearly, the upcoming manuscript is not meant to be submitted to a scientific peer-reviewed journal but to explain the scientific rationale behind **my cry of distress and urgent wake-up call. May they for God's sake draw the world's attention to what I think is now likely to become the biggest and most tragic mistake made in the history of public health in general and in the field of vaccination in particular.**

To support my wake-up call and credibility, I am not nearly as much relying on my credentials (which you can find at LinkedIn: https://www.linkedin.com/in/geertvandenbossche/) as I am on a diversified set of relevant scientific reports from the literature and on the evolution of the pandemic itself. The latter is now featured by the emergence of much more infectious viral variants.

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Nevertheless, you may still opt for now to not believe the statements, conclusions and forecasts that will be made in this manuscript and which have already been summarized as attached. However, I have no doubt that in the days and weeks to come 'doubting Thomas' will have to admit that he was proven wrong. In the meantime, these disastrous vaccination campaigns will likely be intensified and even extended to younger age groups. Given the power, influence and blind ambition of the stakeholders driving these campaigns, it is going to be incredibly difficult to stop this act of complete madness. When all of them will finally have to admit the catastrophic consequences of this 'experiment', precious time and, more importantly, many more lives will have been lost. Eventually, complete lockdowns will likely be imposed for an undefinite period of time as a last resort.

Although largely based on direct or indirect scientific evidence, the views expressed in the manuscript will be my personal views. Of course, I take full accountability of what I am saying and I can only hope that those who're in charge will be sufficiently convinced to take their responsibility and stop all ongoing Covid-19 vaccination campaigns immediately. There should be no excuse and certainly no complaints about lack of warnings by dedicated experts. I cannot emphasize enough that continuing these vaccination endeavors will dramatically prolong, instead of shorten, the current pandemic and take a much higher toll in terms of disease and fatality rates in all of the population. It goes without saying that a such enhancement of this crisis will come with unbearable socio-economic consequences for many years to come.

The manuscript will provide compelling evidence that – as far as acute self-limiting viral infections are concerned - the natural course (i.e., without human intervention!) of a Coronavirus pandemic is typically featured by 3 waves that ultimately flatten as the infection merges into a seasonal 'common cold.' However, it is difficult to predict how long it would take a natural Covid-19 pandemic to 'downgrade' to yet another kind of seasonal 'common cold' without human intervention. Maybe somewhere between 2 to 4 years, but that's a personal guess. This is, of course, not to say that in the meantime one should not do whatever is possible to mitigate the disease in those developing severe symptoms. **But first, "do no harm"** ("primum non nocere"): Given the huge amount of immune escape that will be provoked my mass vaccination campaigns and flanking containment measures, it is difficult to imagine how human interventions would not cause the Covid-19 pandemic to turn into an incredible disaster for global and individual health.

I would have been able to put the appended manuscript together without having dedicated the last 10 years of my career to designing an entirely new vaccine concept that aims at enabling our immune system to kill a multitude of infectious (and even, noninfectious) diseases without allowing the pathogen, or any 'variant' editions thereof, to escape the immune response induced. In contrast, all of the current Covid-19 vaccines rely on strengthening adaptive (as opposed to innate) immunity in general, and humoral (i.e. antibodies) in particular. Hence, none of them will prevent immune escape and, for that matter, all will be subject to anti-viral resistance. Adapting the composition to the new circulating variants does not solve the problem as science tells us that this will even accelerate the rate of immune escape (in asymptomatic Covid-19 carriers).

Isn't it surprising that while we have now become so well aware of all dramatic consequences and threats surrounding microbial resistance to antibiotics, we still don't believe that fighting viruses in ways

that do not completely kill them opens the door to vaccine resistance? While we have been taught to always take the medication for as long as prescribed, even if we were already feeling much better, we still don't seem to believe that viruses can escape to specific antibodies if antibody concentrations or affinity are no longer sufficient to neutralize the virus. Widespread use of antibiotics is generally acknowledged to raise a serious global concern about antimicrobial resistance, but nobody seems to bother about resistance to vaccines that are used in mass vaccination campaigns in the context of an ongoing pandemic. Since those are conducted against a huge infectious background, a multitude of vaccinees will be in the process of seroconverting while being exposed to circulating infectious virus. Prophylactic vaccines against viral or other infectious diseases are typically administered well in advance of a likely risk of infectious exposure. While this is ensuring full-fledged protection to the infectious agent, it is also preventing immune escape and hence, resistance to the vaccine. Aren't we not already witnessing an increasing number of cases of Covid-19 vaccinated people who still shed virus and sometimes even develop mild symptoms? Aren't these cases compelling enough in proving how easily Covid-19 viruses can escape antibody responses? How can we then be so excited about current Covid-19 vaccines knowing that they allow immune escape and thus, enable the virus to select more infectious variants? And do we really think that going for a one dose shot (instead of the prescribed 2-dose vaccination schedule), as some propose, is not going to even expedite immune escape?

In our naïve and simplistic attempt to prevent the pandemic from running its natural course, we are in fact providing the beast with an even much better opportunity to escape host immunity than natural infection does. The only way to do better than the natural pandemic is to *eradicate* Covid-19 right away. To do so, there is probably no other way but to concentrate on vaccination strategies that allow DURABLE priming of innate immune killer cells (i.e., NK cells), the activation of which has already been shown to correlate with full viral clearance in asymptomatically Covid-19-infected subjects. As innate cytotoxic cells enable non-antigen-specific killing of the virus, they don't drive immune escape.

By implementing immune intervention strategies that capitalize on empowering these innate immune cells to acquire immunologic memory, it must be possible to *fully, broadly and durably* protect human populations against *all Covid-19 editions, and even against Coronaviruses at large*. The 'sterilizing' immunity they provide would not only protect people who would 'naturally' become asymptomatically infected (but, unfortunately, only enjoy natural protection for as long as they keep their innate immune system well-trained through moderate but regular pathogen exposure) but also subjects who would 'naturally' develop (severe) symptoms or even succumb to the disease.

In conclusion, fostering the development of NK cell-based vaccines should become a *public health priority*. As will become obvious from the manuscript, NK-cell based hold great promise for stopping this pandemic at its source while also ensuring future preparedness to emerging pandemic threats at large.

G. Vanden Bossche

Immediate cancellation of all ongoing Covid-19 mass vaccination campaigns should now become *THE most acute health emergency of international concern*.

Executive summary (see also slide appended on p.6 below)

The manuscript, which is in now in the process of being finalized, should shed some light on how the virus and especially its interaction with the host immune system determines the *natural* course (i.e., *without* human intervention) of a Coronavirus (CoV) pandemic. The interplay between host immune defense and viral immune escape determines the course of a natural CoV pandemic (including a natural Covid-19 pandemic).

In the clinic, viral immune escape is known to occur when the neutralizing capacity of serum antibodies (Abs) does not suffice to fully eliminate highly mutable viruses (e.g., CoV) for lack of their concentration or affinity. In a CoV pandemic setting, seroconversion occurs against a background of high infectious pressure and is, therefore, prone to promote viral immune escape.

The first wave of disease[1] (and mortality) primarily affects elderly people (or otherwise immunocompromised subjects). *Selective* (i.e., adaptive) immune escape is expected to cause this wave to transition into a more severe, second wave in younger age groups. Subsequently, *non-selective* (i.e., innate) as well as *selective* immune escape operated by increasingly infectious viral variants will trigger a third wave. The latter would primarily affect subjects who recovered from disease they contracted during the first wave as their seroneutralising Abs do no longer properly match the new circulating viral variants. This third wave of disease (and mortality) would come to an end when those who recovered from the disease will have mounted new functional Abs against these immune escape variants. As seroconversion in this population will now occur much faster (due to recall of cross-reactive T helper memory cells) and as the majority of the young and middle-aged population will either be seronegative or have seroconverted already by the time the third wave starts to expand, chances are slim for the virus to escape the host's Ab response. Asymptomatic[2], seronegative individuals (i.e., the vast majority of young and middle-aged people) may spread virus upon (re-)infection and hence, constitute a relevant source of viral transmission. However, CoV infection in these asymptomatic carriers is abrogated after a short period of viral shedding. Viral clearance in these subjects is likely to occur through activation of NK cells. The latter are capable of recognizing CoV-associated, antigen (Ag)-nonspecific patterns on the surface of CoV-infected epithelial target cells. As killing by NK cells is, therefore, not Ag-specific and as seroconversion

[1] For the purpose of the manuscript, 'disease' refers to *severe* Covid-19 disease with involvement of lower respiratory airways

[2] For the purpose of the manuscript, 'asymptomatic' infection refers to CoV infection which does not cause clinically relevant symptoms or only causes a mild level of disease (i.e., only involving upper respiratory airways)

in asymptomatically infected subjects is only short-lived, viral immune escape does not normally occur. Consequently, new, more infectious, variants are unlikely to emerge from this population as long as viral infectiousness does not dramatically increase.

At the point of 'no immune escape', the pandemic will be under control and merge into an endemic infection. However, as long as the point of 'no immune escape' isn't reached, any additional immune selection pressure, for example as a result of suboptimal concentration or affinity of Ag-specific (e.g., spike protein-specific) Abs, will allow the virus to rapidly unfold more infectious, immune escape variants. Additional immune selection pressure, especially when exerted during the second wave of a CoV pandemic, is likely to precipitate and amplify viral immune escape. This might even cause the second and third wave to merge into a single huge wave of mortality and disease that affects all layers of the population (possibly, with the exception of small children).

Especially mass vaccination campaigns, particularly when conducted in the midst of a pandemic, are prone to exerting enormous immune pressure on circulating virus strains. This is because the vaccine is used in an increasingly infectious context (as escape variants are more infectious). Mass vaccination campaigns will accelerate the emergence of even more infectious immune escape variants. This because the number of vaccine recipients who seroconvert within a given time period will dramatically increase[3]. In addition, Ag-specific, high affinity Abs induced by any of the current vaccines will outcompete natural, *broadly* protective mucosal IgM antibodies as the latter only bind with low affinity to the receptor-binding domain of CoV (RBD). This will particularly affect natural resistance of younger age groups which - thanks to a well-trained innate immune system- resisted disease during the first wave. The new circulating CoV variants may now even be able to escape the host's CoV variant-nonspecific line of immune defense at the mucosal portal of entry. These age groups may, therefore, become more susceptible to symptomatic infection and shedding caused by more infectious variants.

But mass vaccination campaigns will also have severe consequences for those who got vaccinated first (mostly the elderly or people with underlying disease or those who are otherwise immunocompromised). In the highly likely event that mass vaccination will soon result in antiviral resistance (see below), these people will have no single bit of immunity left to rely upon. In contrast to the infectious circulating virus, current vaccines do either not contain any critical killer cell motif or fail to activate dedicated killer cells. It goes, therefore, without saying that vaccine-induced immune responses will inevitably result in a dramatic enhancement of morbidity and mortality rates in *all* of the human population (except for small children?).

[3] Alike naturally infected subjects, vaccine recipients need time to mount a full-fledged Ag-specific Ab response

Further to all of the above, low exposure to circulating CoV strains (e.g., due to stringent containment measures) will increasingly weaken innate mucosal immunity for lack of training. Again, this is particularly relevant for those who - thanks to their sufficient and adequate innate immune defense – got away with asymptomatic infection during the first wave. Stringent and widespread infection prevention measures are now increasingly compromising their innate immunity and rendering them more susceptible to symptomatic infection. Especially the younger age groups may, therefore, end up with relatively higher morbidity and mortality rates, even regardless of the emergence of more infectious viral variants. This is to say that broadly implemented infection prevention measures will only amplify the already detrimental consequences of ongoing mass vaccination campaigns. It is reasonable to assume that the combination of non-selective and selective immune escape will cause morbidity and mortality rates in younger age groups to explode.

The more Covid-19 vaccination campaigns in the young and middle-age groups will be delayed (i.e., relative to their initiation in the elderly), the more they will enhance morbidity and mortality rates in this group: By the time mass vaccination campaigns are about to start in the young and middle-aged groups, a substantial number of these people will already have been infected with Covid-19. Enhanced rates of infection by highly infectiousness viral variants significantly has now increased the likelihood for them to become re-infected while being in the process of seroconverting. So, by the time vaccinations will be initiated, viral immune escape in this group may already be fueling a vicious circle of enhanced viral infectiousness resulting in more seroconversion and hence, more immune escape. Mass vaccination campaigns in this group will only dramatically deteriorate the situation as they will lead to a fast and massive increase in the number of asymptomatic subjects that are in the process of seroconverting against a highly infectious background. and, therefore, prone to promoting viral immune escape. As there is naturally no reason for them to isolate, there will be plenty of opportunity for the highly infectious circulating strains to replicate in the presence of suboptimal Ab titers and, therefore, to escape the host's immune control.

Hence, the more vaccination campaigns in this group get delayed, the more selection of even more infectious viral variants will be expedited. The ensuing exponential increase in viral immune escape rates will ultimately enable viral variants to even break through vaccine-mediated protection in the vaccinated elderly. As their Abs increasingly mismatch the ever more infectious emerging variants, they will no longer manage to control viral replication and shedding and rapidly allow for massive viral immune escape. Because seroprotective Abs primarily confer protection through targeting Covid-19's RBD, the virus will now increasingly select mutations in this particular part of the spike protein as those most readily enable the virus to escape vaccine-induced Abs. This will inevitably precipitate resistance to the vaccine. As

a result of mass vaccination, people who got the vaccine first will suddenly no longer be protected and, despite vaccination, fall prey to a wave of catastrophic morbidity and mortality.

There can, therefore, be no doubt that current vaccination strategies are rendering the impact of mass vaccination campaigns even more catastrophic and only adding to the magnitude of a pending global health disaster. However, mass vaccination also harms individual health as vaccine-induced variant-specific Abs will outcompete natural variant-nonspecific mucosal Abs for binding to CoV variants and thereby deprive individuals from their broadly protective natural (life)line of immune defense.

As large scale vaccination campaigns combined with the sustained implementation of several containment measures will only expedite the occurrence of viral escape mutations, the illusory hope that current Covid-19 vaccines could generate herd immunity should once and for all be thrown overboard. Along the same line of reasoning, it is not unthinkable that Covid-19 will, once again, cross species barriers. One can definitely not rule out that with growing immune-mediated selection of virus variants, Covid-19 is ultimately going to be able to jump to other animal species, especially industrial livestock (e.g., intensive pig and poultry farms with high stocking density) as i) these species are already known to host several different Coronaviruses and ii) variability/ mutations in the very same spike protein, and particularly in the RBD, are known to be responsible for shifts in host tropism/ susceptibility. Similar to the situation with influenza virus, these animal species could then constitute a reservoir for SARS-COVID-2 virus. Depending on the prevalence of circulating animal CoVs in those farms (and hence, the level of trained immunity), those animals could now serve as asymptomatic carriers, thereby constituting a serious threat to humans.

Conclusion:

The combination of mass vaccination and infection prevention measures is a recipe for a global health disaster. Following the science, one has to conclude that all age groups (possibly with the exception of small children) will be heavily affected and subject to rates of morbidity and mortality that raise much faster and much higher than those expected to occur during the *natural* course of a CoV pandemic. This will particularly apply if the sequence of mass vaccinations following the first infectious wave parallels that of natural infection (i.e., immunocompromised people and elderly first, followed by the younger age groups).

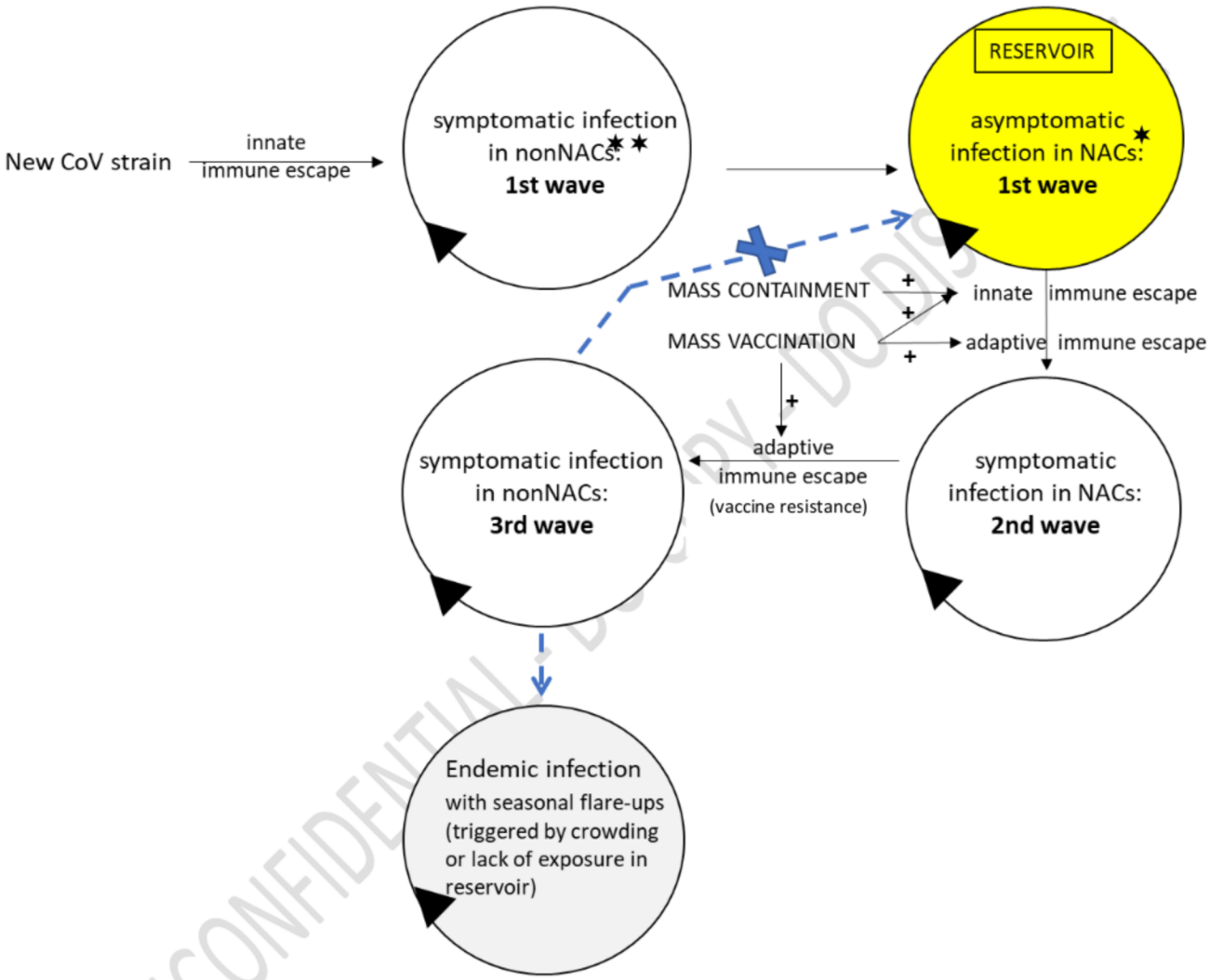
No one, for that matter, should be granted a right to implement large-scale pharmaceutic and non-pharmaceutic immune interventions, especially not during a viral pandemic, and certainly not without an in-depth understanding of the immune pathogenesis of a viral pandemic. When one follows the science, and nothing but the science, it becomes extremely difficult to not label

ongoing mass vaccination campaigns as a crime, not only to public health but also to individual health.

To substantiate the reasoning above, the manuscript will first explain how components of the innate immune system can protect against Covid-19 and render infections asymptomatic. It will then go on to explain in more detail why and how, in an immunologically Covid-19-naïve population, selective (i.e., adaptive) immune escape shifts the first wave of disease and death from the elderly (and immunocompromised) subjects to those who at the outset of the pandemic got away with asymptomatic infection (i.e., the younger and middle-aged population segment). Similarly, it will be explained how viral immune escape in the asymptomatically infected population finally shifts back the burst of morbidity and mortality to the elderly, and how the population eventually controls the pandemic by controlling viral immune escape. This will already illustrate the critical importance of desiccating the changing contribution of innate and adaptive immunity to the population's overall immune defense against a viral pandemic. Understanding these dynamics helps to comprehend the sophisticated course of a natural CoV pandemic, how it eventually merges into an endemic infection and why human intervention has a highly detrimental impact on the refined interplay between the virus and its host. In regard of the latter, the devastating global health impact of ongoing mass vaccination campaigns and accompanying stringent and widespread containment measures will be explained in more detail as the global and individual health consequences could simply be unbearable for many years to come.

After the introductory section on innate immune defense mechanisms relevant to Covid-19, other relevant topics will be addressed in form of questions and answers. Last, a section will be dedicated to the scientific rationale for using NK cell-based vaccines that could provide sterilizing immunity and hence, wipe out Covid-19 and related variants all together.

The natural course of a CoV pandemic is controlled by the population's innate and adaptive immunity and dramatically aggravated by antibody-based vaccines when used in mass vaccination campaigns conducted in the course of the pandemic and flanked by stringent containment measures



✶NAC: Natural asymptomatic carrier : for the purpose of this manuscript, NAC is defined as a subject disposing upon a level of innate immunity high enough to resist disease

✶✶nonNAC: For the purpose of this manuscript, nonNAC is defined as a subject who is not endowed with a level of innate immunity high enough to be able to resist disease when exposed to infectious virus during the first wave