CoVID-19: Lessons for Policies ǂ

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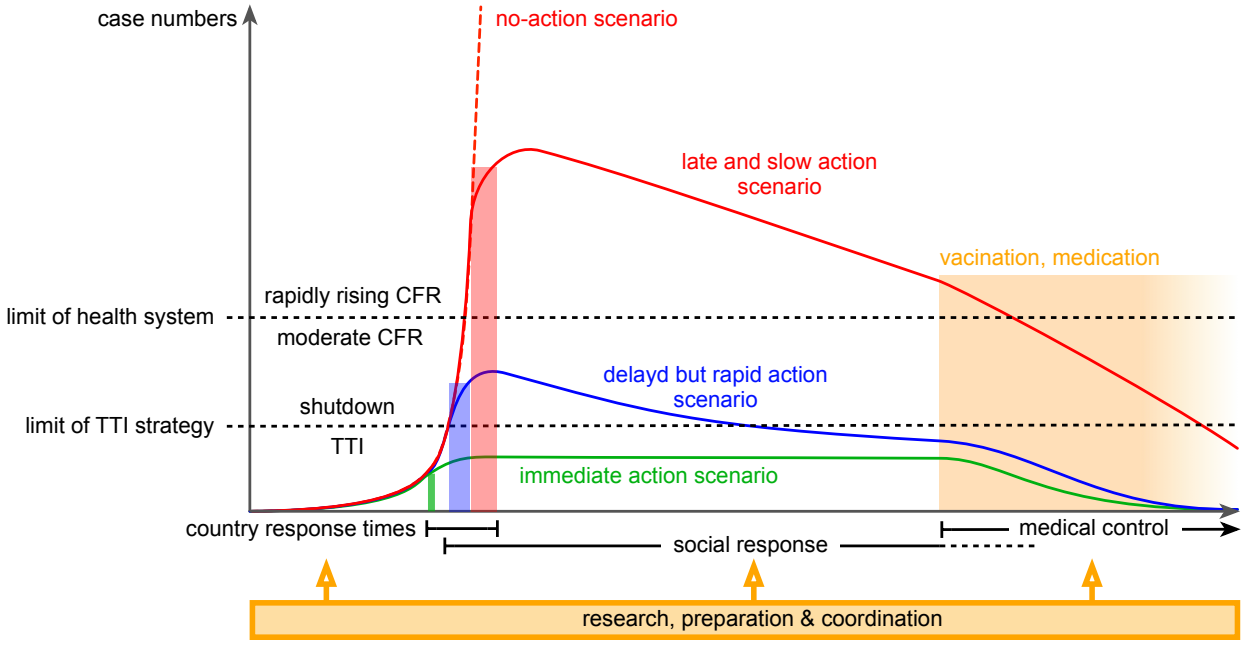
Abstract

In spite of the warnings, the current CoVID-19 pandemic took the world by surprise: in just four month, it conquered the globe, claimed over 200'000 lives and the unprecedented governmental actions impact about half of the world population. The resulting economic meltdown is expected to eliminate globally 9 trillion USD in 2020 and 2021 alone, the size of the yearly GDP of the world's 150 smallest economies. The resulting crises might cause mass-unemployment and a hunger pandemic later this year. This report identifies a set of policies minimizing both loss of lives and economic costs. Key-statements are:

1) The CoVID-19 pandemic will last for at least two more years. This is the minimum time required for a vaccination campaign to safely reach sufficient numbers of people.

2) A tracing, testing & isolation (TTI) approach is the best strategy to minimize both, the pandemics economic burden and fatalities. It requires a combination of cost-efficient measures and international coordination for best effect.

3) To prevent such pandemic outbreaks in the future, several neglected research areas require a funding boost. Just 1% of the bill of the current crisis could support the research of 45'000 scientist for 20 years.



ǂ This document is an updated summary of a recently published essay. For the full report see: J. Eppinger, M. Rueping, CoVID-19: Where We Are, What We Should Do and What We Should Learn. *Preprints* **2020**, 2020040484. (www.preprints.org/manuscript/202004.0484/v1; doi: 10.20944/preprints202004.0484.v1)

1) Current Situation

Despite repeated previous outbreaks of zoonotic viruses (figure 1) as well as warnings of scientists and international organizations that pathogens striving in animals constitute a nearly unlimited reservoir for potentially catastrophic pandemics, the zoonotic SARS-CoV-2 hit an unprepared world[1].

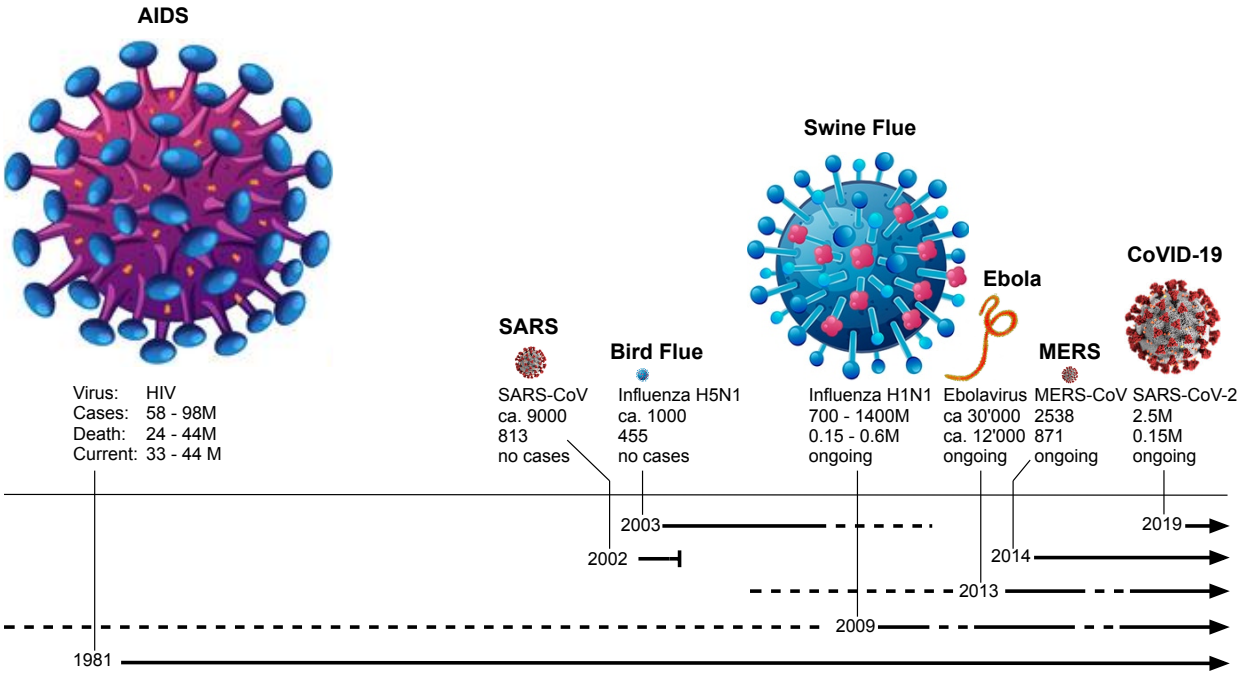


Figure 1. Overview of major outbreaks of zoonotic viruses during the last four decades. The virus particle sizes roughly represent the pandemic impact until April 2020.

Today, just four month after the first identified cases, CoVID-19 has conquered the entire world except a few remote places and the numbers of confirmed cases approaches 3.5M with over 230'000 fatalities attributed to the pandemic. However, even if hidden figures [2] are taken into account, only between 0.04 and 0.2% of the global population have been infected so far. While the current rate of 80'000 daily new confirmed cases imposes a substantial strain on health systems, the world's population grows at a nearly threefold rate. Eradication of the global CoVID-19 pandemic will require immunization of more than 4.5 – 6 billion people (R_0 of 2.24 – 3.58 [3]). At a current case fatality rate (CFR) of over 4 % [4] such a "heard immunity" goal can only be achieved either by accepting a global toll of at least 200M fatalities or through a vaccination campaign. Realistically, the introduction of a SARS-CoV-2 vaccine is more than nine months away, and a global vaccination campaign might take one or two more years to reach the numbers required. Accordingly, pandemic control measures will be kept in place beyond 2021 to avoid exponential propagation of infection among the non-immunized population.

It must be understood that due to the exponential nature of the pandemic a balanced middle course, between either a fully established wave with hundreds of million fatalities within less than a year or a stringent pandemic control, does not exist.

Currently, pandemic control through governmental restrictions impacts between 1/3rd and 1/2 of the global population [5]. The distress of pandemic containment measures on the world's economy is estimated to cost 9 trillion USD within the 2020/21 two-year period [6]. Yet, that might be a conservative estimate, if vaccine development and introduction encounter difficulties. The pandemic-inflicted economic downturn will cause fatalities through many contributing factors including unemployment, general GDP decline [7], reduction of spending on health care or loss in agricultural productivity as well as immediate effects. The UN estimates that 369M children in 143 countries do not have access to school lunches anymore and the WFP warned of a "hunger pandemic" as in the wake of CoVID-19 induced shutdowns additional 135M people might be pushed to the brink of starvation this summer [8].

2) A Policy to Reduce Loss of Lives and Economic Costs.

As we detail in a recent report [4] it is evident from current pandemic data that a testing, tracing & isolation (TTI) strategy is superior to other approaches. Scientists from the Max-Plank Society, and Frauenhofer, Helmholtz and Leibnitz Institutes just summarized the same conclusions in a joint statement [9]. TTI-based policies minimize both, the pandemics economic burden and fatalities. Importantly, this strategy does not trade between economic and health considerations. To make it work effectively it needs to be supplemented by actions on the governmental and personal level. In brief, TTI policies should combine:

1. Core measures on a governmental level:
    a. fostering **testing** capacities and supply of required resources
    b. identification of infected and retrospective **tracing** of contact population
    c. **isolation** of infected persons and all contacts until test results are available
    d. where infection chain tracing fails, **quick local** implementation of shut-down measures [10]
2. Associated measures and restrictions on a governmental level:
    a. **international coordination** of measures
    b. **clear communication** and explanation of measures
    c. **restriction of large gatherings** until fast mass testing is available
3. Measures on a personal level:
    a. **masks** whenever in contact with persons outside of the household
    b. **social distancing** measures
    c. **personal hygienic routine** e.g. hand washing after outside contacts and frequent disinfections of surfaces

The combined measures reduce the reproduction rate R_0 to or below 1. Depending on technological capabilities (testing capacities vs. tracing depth) and cultural background (e.g. habitual social distance) the contributions of individual measures will vary from country to country. Testing & tracing can be balanced to fit regional needs and preferences. A low tracing depth requires higher testing capacities and vice versa. This balancing degree of freedom reduces costs of a TTI policy, which therefore might even be adaptable to low income countries. The richer economies should come to the conclusion that installing and maintaining essential CoVID-19 testing facilities in poor countries is cheaper than a constant spillback of infections or measures to avoid them. It is even possible to achieve near normal life conditions [11] without any tracing, if daily 45'000 test per 1M population can be conducted in accordance with a focused testing scheme.[12] The required technology is currently under development. [13] Installation of fast mass-testing capabilities should even allow opening of large events like soccer games as well as unrestricted international travel and exchange, which otherwise may resume only, if tracing beyond borders is established. The international exchange of data collected from citizens is a delicate topic. Exchange might just involve the inter-country notification that a recent visitor was found to be infected, or a person had a positive contact while visiting. Further tracing can rely on in-country data.

It must be understood that the CoVID-19 pandemic is global matter, which mandates worldwide coordination of actions. The lack of an international strategy is devastating, since it extends the duration of pandemic waves in individual countries (thus increasing case numbers and fatalities); generates viral pockets from where infection can resurge; and causes unnecessary economic distress impacting countries, which have reacted with quick and efficient measures. E. g. the disruption of globalized production processes and trade networks caused this April a 24.3% drop of exports from South Korea, despite this countries ability to avoid shut down due to consequent TTI.

3) Policy Implications for the Future: Research Funding for Neglected Pandemic Research

The world's global research budget amounts to $1.7T per year [14], which is about one fifth of the $9T economic damage the CoVID-19 crisis will cause during the next two years. Just 1% of the estimated pandemic price tag could support the research of 45'000 scientist for 20 years (figure 3). This calculation doesn't even factor in that money spent on research usually generates economic return from products developed surpassing the initial R&D costs. In comparison, the $109 billion yearly global R&D budget spent on health is dwarfed by the pandemic related costs.

However, profit-oriented companies support the majority of the R&D expenses. Yet, research into pandemic related problems most of the time cannot generate a product that pays for its development cost, because pandemics are unpredictable one-time events. Considering the potential devastating pandemic burden, taxpayer's money should be allocated. The following non-complete list compiles neglected research areas, where an increased research budgets could give the world a head-start in future pandemics:

1) global pandemic plans and models
2) emergence of zoonotic viral diseases
3) vaccination
4) antibiotics
5) pharmaceuticals targeting zoonotic viruses (other than influenza and HIV)
6) cheap and adaptable viral exposure test
7) infrastructural requirements, e.g. GMP manufacturing processes and cold chain tracing [15]

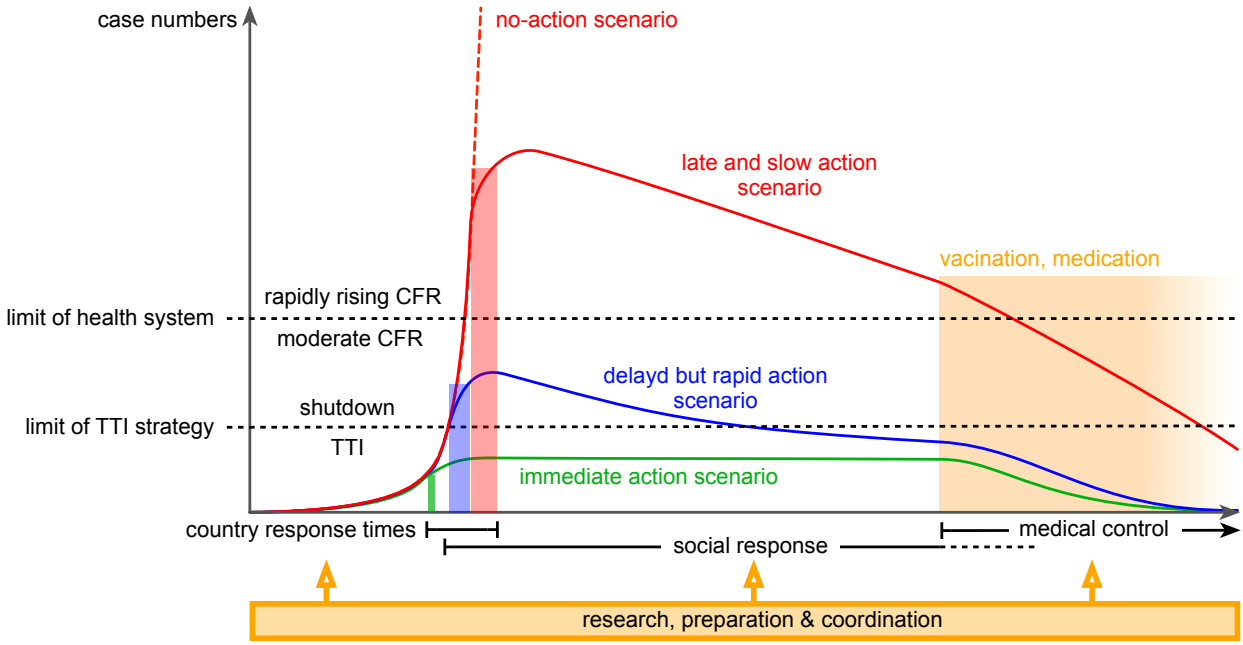


Figure 2. Illustration of the influence enhanced funding for neglected pandemic research on pandemic mitigation. Reduced reaction time results on lower case numbers and CFR as well as economic impact. Earlier onset of medical pandemic control through medication and vaccination will dramatically attenuate a pandemic's aftermath.

Since in non-pandemic times, over 70% of the world's population die of non-communicable diseases (NCDs) like cancer, diabetes, cardiovascular, stroke, Alzheimer's disease or even obesity,[16] the pharmaceutical industry has to focus on NCDs, which subsequently funnels a lot of public research funding and academic research in that direction. Hence, publications with another focus are not well cited and scientist in that field cannot advance, which further reduces their dim funding opportunities. A substantial increase in governmental funding is required to sustainably change the situation. Available funding attracts scientist to work in an area, even if publications are not among the most highly cited. Larger numbers of active researchers will slowly but steadily increases the appeal of the field for others since the growing community guaranties higher impact.

Vaccine Development. While vaccines are among the most cost-effective and beneficial developments for public health [17], development costs involving clinical trials are extremely high and the major markets are in low-income countries. Even in rich economies, financial returns are usually minimal and the economic and research risks are great.[18] Most vaccination campaigns only exist due to private or public initiatives. Today, the lack of previous research leads to a markedly prolonged vaccine development time. Besides deficiencies in vaccination-related knowledge, many substances are required for a vaccine formulation, and each one needs to undergo lengthy authorization procedures. Several substances for vaccine formulations were approved back in the first part of the last century, while new promising methods like *m*RNA vaccination rely on new ingredients, which in most cases are not yet approved.

However, it must be warned against trading established regulations for safety to accelerate development in the current situation. Side effects due to release of not well-tested vaccine candidates might prove highly counterproductive for the acceptance of vaccination campaigns in the future.

An additional complication arises from a strong publication bias in academic research. The full development of a functioning vaccine reaches far beyond the capacity of academic research groups as a complex mix of interdisciplinary expertise is needed; a plethora of testing methods and regulations are required; and finally costs rise exponentially during the progressive stages of such a project. Thus, many studies suffer from a low reproducibility, superficiality or even data fabrication. A recent review summarized the situation as follows: “low reproducibility of the currently published outcomes, especially, in drug development field, resulted from the inappropriate designs with little practical rationality combined with the positive result-oriented publishing bias and the misconception of “research for publication”, sets up also a huge barrier to translation of bench work to bed therapy” [19]. Another investigation of the publication system in the medical field concludes: “The production of systematic reviews and meta-analyses has reached epidemic proportions. Possibly, the large majority of produced systematic reviews and meta-analyses are unnecessary, misleading, and/or conflicted.” [20] Clearly, publication bias is a result of the current funding system and is detrimental to the field. More available resources, allowing academic researchers to focus on long-term high quality dissemination rather than on high quantities should reduce the problem.

Pandemic Models and Response Plans. The slow implementation pandemic response left shutdowns as the only option for containment. Hence, in the current early phase of the CoVID-19 pandemic hesitant action is the primary cause for high fatality numbers and unprecedented economic costs. Since a two-week difference in response time has a substantial effect on the course of a pandemic [4], clear-cut pandemic response plans including a systematic and globally coordinated are required. Such plans should include model predictions detailing the reduction of transmission rates through individual measures for a given transmission path and taking the cultural background of the population into account. Also, the technologies for all potential actions need to be available, or even better in place, and their use should be in agreement with governing laws. If actions were globally coordinated, swift and tailored implementation of selective measures could prevent the world from slipping into the next pandemic. Global coordination based on a pre-established plan would circumvent unproductive finger-pointing and egoistic actions in the future.

Antibiotics. Multidrug resistant bacterial strains pose a growing pandemic threat. According to a recent CDC report, more than 2.8 million antibiotic-resistant infections occur in the U.S. alone each year, and more than 35,000 people die as a result [21] and mortality and morbidity from resistant infections is on the rise globally. However, due to associated economic risks the pipeline for new antibiotics is running dry as that the vast majority of the large pharmaceutical companies have exited the field. Sales of a new antibiotic can not support its development costs, since “Sales volumes are limited by the short treatment duration inherent in antibiotic therapy, and local antimicrobial stewardship programs are increasingly restricting the use of antibiotics. A truly novel antibiotic would likely be reserved for rare infections caused by the most highly resistant strains of bacteria” [22]. And a myriad of other economic, regulatory, and scientific barriers exists, too.

In summary, governmental and privately funded projects are currently our best hope to prevent catastrophic pandemic waves in the future. If governments don’t step forward with heavy investments into R&D targeting pandemic threats, the current CoVID-19 episode might just be the prelude to a much worse global era. Because one thing is for sure: the next pandemic will come!

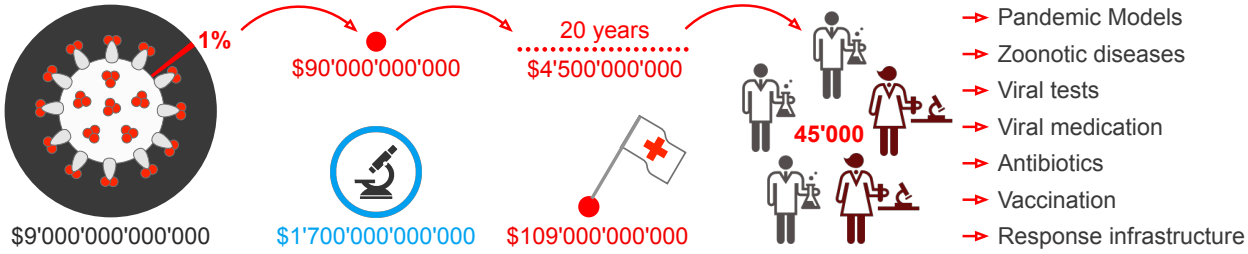


Figure 3. Comparison of CoVID-19 cost with global annual R&D spending and the amount of that spent on health R&D. Just 1% of the bill of the current crisis could support the research of 45’000 scientist for 20 years.

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[2] Small scale studies from Germany and Austria seem to suggest that only one in five cases might be detected since test capacities are limited. However, the results should be taken with care, at least the German study is currently debated due to methodological concerns. See: www.land.nrw/sites/default/files/asset/document/zwischenergebnis_covid19_case_study_gangelt_0.pdf; https://www.medinlive.at/wissenschaft/stichprobentests-infektionen-bei-vielfachem-der-offiziellen-zahlen

[3] Zhao, S. *et al. "Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: A data-driven analysis in the early phase of the outbreak." Int. J. Infect. Diseases* **2020**, *92*, 214 – 217.

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[5] www.statista.com/chart/21240/enforced-covid-19-lockdowns-by-people-affected-per-country/

[6] www.imf.org/en/News/Articles/2020/04/14/tr041420-transcript-of-april-2020-world-economic-outlook-press-briefing

[7] a positive correlation of GDP and life-expectancy is known as the „Preston-Curve, for a recent analysis of contibuting effects, see: W. Lutz, E. Kebede. *„Education and Health: Redrawing the Preston Curve". Pop. Dev. Review* **2018**, 44, 343 – 361.

[8] www.wfp.org/news/wfp-chief-warns-hunger-pandemic-covid-19-spreads-statement-un-security-council

[9] https://www.mpg.de/14760567/28-04-2020_Stellungnahme_Teil_02.pdf

[10] The pandemic development in Japan demonstrates the importance of quick local shutdown measures, if infection chains cannot be followed anymore. While the Japanese TTI approach kept infection rates at a very low level from January till end of March, case numbers were starting to grow exponentially as soon as in early April infection chains could not be tracked anymore. Only after a delayed declaration of emergency on April 7th case numbers started to decline roughly weeks later. Quick local shutdowns could have prevented the exponential spreading earlier causing significantly less economic distress.

[11] Family events, smaller birthday parties and even visits of theaters should be possible, if measures on the personal level are followed appropriately. However, the super-spreading capacity of large events and gatherings has proven to be lethal and quickly boost the CoVID-19 reproduction rate. Hence, such events can only take place again after a sufficient level of immunity is reached or fast-mass testing capabilities are established.

[12] A manuscript detailing the correlation of pandemic reproduction rates with testing capacities and tracing depth is currently in preparation.

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[14] uis.unesco.org/apps/visualisations/research-and-development-spending/

[15] For WHO recommendations on vaccine management, see: www.who.int/immunization/programmes_systems/supply_chain/evm/en/index1.html. For cold chain requirements in vaccination campaigns, see: www.who.int/immunization/documents/IIP2015_Module2.pdf

[16] www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases

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