Editorial

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Survival of the Wealthiest?

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A number of promising Covid-19 vaccine candidates may pass approval this month. However, the pandemic will only be brought into check through an equitable, epidemiologically informed distribution policy. The health emergency provides a unique opportunity for a new paradigm to mitigate between global health, national and commercial interests.

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The contributions that researchers have been making to mitigate the impact of the pandemic have been decisive, given the many research programmes that have been badly disrupted. The demonstrable fact that basic and clinical research rose to the challenge with unprecedented energy, and efficiency should unequivocally underscore the value of the research system. We see this in our community of biomedical researchers, and it is also true for the humanities, social sciences and engineering.

One remarkable development is the rapidity with which a large number of SARS-CoV-2 vaccines are moving into clinical tests. Nonetheless, the development of robust vaccines is just an early step to global protection, and we still see recurrent problems that existed before the pandemic and are likely to persist unless they are addressed decisively now in our hour of need. Let's not miss this critical opportunity as new vaccines, diagnostics and drugs are being introduced to combat COVID-19.

Our foremost concern is equitable access which must be dealt with immediately, before any vaccine is licenced for distribution. Particularly for vaccines, the moral and public health imperatives for fair and effective distribution, respectively, cannot, and should not, be disentangled. The profound global impact of the pandemic has led to an unprecedented parallelization of national, academic and commercial efforts to develop vaccines for COVID-19 but we cannot know yet which of these will be effective, nor which project will in fact ultimately deliver the biggest impact against the pandemic through optimal distribution and access. Thus, health planners are forced to stake a bet, making constructive global health planning hard.

At the same time, a known obstacle to the development of vaccines (and other drugs, particularly antibiotics) is that these are employed only once or a few times per patient. Even for a for-profit company with the best intentions, this is not necessarily a sustainable business model. Further, even the least expensive vaccines may be too expensive for developing regions. Under conditions of guaranteed high demand for a vaccine, as in the case of this pandemic, a firm would find it hard to resist exploiting its position for profit. To their credit, pharmaceutical companies involved in COVID-19 vaccine development signed a joint letter stating that any vaccine will be made accessible to poorer nations via COVAX, apparently in response to their perception of a mounting risk of national interests dominating the global health response. Indeed, the same challenges apply at national level, where "our citizens first" is more readily sold to an electorate, even if scientific advice clearly recommends a global vaccination approach.

Whether or not national or commercial interests dominate the COVID-19 response remains open. For one, there are multiple vaccine candidates from several companies and nations close to approval. Nonetheless, even in the best-case scenario that a dozen vaccines are shown to be effective, global demand will outstrip supply for at least another year, with initial annual global production estimated at a little over 2 billion doses.

This is a critical moment to reflect on these issues, certainly also in the context of other vaccines for more localized diseases with high or even higher fatality rates. During the days of optimism for an HIV vaccine, it was assumed that rich regions would need to support poor regions to buy vaccine doses, but the scale was orders of magnitude smaller. The question now is, do we accept the idea that vaccines have a cost that keeps pharmaceutical companies incentivized, but that only the rich or countries with well supported health systems can afford? If we allow deregulated market forces to set the price, can we hope to find a way to subsidize global access? Notwithstanding some notable exceptions like China and Russia, after decades of delegating antibiotics and vaccine research to private institutions, only big pharma can currently provide a rapid, scalable response to a global health emergency.

Consequently, one alternative in particular for Europe, Japan and the USA would be to remove a profit motive by at least temporarily nationalizing the relevant branches of the industry. After initial moves to purchase promising vaccine biotech companies failed, governments now back vaccine development through public–private partnerships and guaranteed advance orders, which reduce the risk

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of developing an ineffective vaccine for companies. For example, the US National Institutes of Health Bumpers Vaccine Research Center is partnering with Moderna; the German government has a stake in CureVac. Meanwhile, in the absence of suitable local Pharma infrastructure, the Chinese and Russian governments are running their own vaccine programmes.

But should this mean that any of these governments gets the first batches of the vaccines they supported? The USA and the UK alone are reported to have already pre-purchased 1 billion doses from various providers Moderna. In Europe, the EU has stepped in by acquiring 800 million doses with an equitable distribution policy among EU member countries, and today announced pre-orders of 300 million doses of the BioNTech-Pfizer vaccine after encouraging initial phase 3 trial results. Even in an open market, should rich entities—whether governmental, private, or non-profit—be able to buy vaccines first-come first-served? Of course, all of this is happening against a background of global Realpolitik, not to mention human nature: there are few if any no-strings attached transactions at the highest government levels and countries are likely to leverage political gain from those in particular need for vaccination.

We might compare this to the recent roll-out of a fast, inexpensive SARS-CoV-2 antigen test made possible by a partnership between WHO, the European Commission, the French government and the Gates Foundation. In return to guaranteeing the companies involved (SD BioSensor and Abbott) a minimum purchase volume, the companies guaranteed distribution of 20% of the overall production to lower- and middle-income countries. Whether this distribution ratio is informed by medical need or a commercial compromise is another matter. Another comparator is the initial publication by Christian Drosten and his colleagues of a real-time PCR diagnostic test, including workflow details, in January of this year. This allowed the WHO to distribute at least one-quarter of a million kits within a month of that publication. As far as anyone knows, no one claims "ownership" of this globally used test.

Could this model work for vaccines as well? We would point to the "Imperial College vaccine" project, which is intended for royalty-free distribution in low-income countries through VacEquity Global Health. One early lesson might be taken from the development of the "Oxford vaccine" which appears to be relying on the Serum Institute of India and AstraZeneca, both private companies, for scale-up. The head of Serum Institute has indicated initial distribution would split 50/50 between India and, via GAVI, to low-income countries. One can argue whether or not this is equitable, but at least it begins to dent the larger problem of fairness of distribution. More generally, the COVAX group (CEPI, GAVI and WHO) has announced it intends to distribute 2 billion doses, "regardless of ability to pay" to its member countries, which includes 64 industrialized and 92 lower GDP nations; it would be critical that this purchasing power does not create a contest with national and regional purchasing programmes. COVAX could in principle work as a good balance to economic or national-focussed forces, but its funding struggles to balance the buying power of large Western nations, and 2 billion doses translates into vaccination for 3% for the population of the member countries—well below herd immunity. This would indicate in any case that the funding, however large it is, will still struggle to balance the buying power of particularly wealthy nations. One legitimate criticism levied at COVAX is its rigid geographical distribution key, which does not take into account optimal global health impact and the respective medical or economic needs of member countries—likely this was the price to get agreement for COVAX, which remains a tremendously important achievement in these days of typically introverted policy priorities.

As Tedros Adhanom Ghebreyesus, head of WHO, noted in a stark warning against "vaccine nationalism": "when we have an effective vaccine, we must also use it effectively. And the best way to do that is to vaccinate some people in all countries rather than all people in some countries". UN Secretary-General Antonio Guterres added, "A vaccine must be global public good. Vaccines, tests and therapies are more than life savers. They are economy savers and society savers". Thus, the second reason to put global health above national interest is that this guarantees the pandemic does not undermine peace and global prosperity. In light of this, why would countries make national interest subservient to global interests?

It is essential to make binding decisions now, and not to continue debate into what is likely to become an extremely turbulent time when the first vaccines become available early next year. In principle, the WHO should take the lead and member nations commit to a joint declaration of equitable global vaccine access. But, given the myriad needs and priorities its member states have to deal with, it may be an overwhelming task to prioritize global health over national emergencies. Declarations are one thing, but on-the-ground decisions will only carry weight if they are supported by national law. Notably almost half of the world's nations (90) have asked to WHO for assistance in procuring SARS-CoV-2 vaccines for them, something the WHO is not in any way funded to achieve.

Deciding where to distribute the first doses of available vaccine must rely on data-driven evidence that carefully weighs the tension between lowering mortality or spread of the pandemic and, equally, the tension between reducing premature death in the at-risk population and protecting essential workers to sustain health systems and the economy. Each infectious disease requires a different response, so we cannot rely on the previous playbooks from, for example, emerging influenzas. There seems to be agreement that "frontline" or "essential" workers should be first. But how are these groups defined? In Germany alone 4 million (5%) work in the health sector. And after this, deciding on a priority for vaccination is even less straightforward: is it to keep younger people able to keep economies going? Is it older people who are more likely to suffer severe effects of the disease? "Underlying conditions" is not a rarity and will we need to make decisions on which underlying condition is more worthy of protection? Can we take account of the significant number of patients with long-term effects ("long tail" COVID-19)? In rich Western countries, up to half the population may be at risk, possibly in contrast to sub-Saharan Africa and India, where, based on the data available, death rates may be considerably lower. In that sense at least, and assuming the data are comparable and reliable, any vaccine distribution asymmetry may in principle be buffered by the higher susceptibility to the virus in richer countries.

But one area where a large intergovernmental organization is uniquely placed to act is to set up large standardized databases to epidemiological research. In our current situation, particularly in Europe, this would require care to protect data—interacting national COVID-19 warning apps are a case

in point. But this is a problem that can be solved. Every step in vaccine development, including being able to understand the efficacy at a population level, will require data gathering and sharing. There is already some data science on this but, again, knowing ahead of time what and when exactly the paths to full vaccine coverage will be, will be a critical public health decision.

These decisions cannot be made centrally by the WHO or the UN, given the immense national heterogeneity. A formidable challenge is therefore to balance national public health prioritizations with an equitable international distribution of vaccine doses.

We should also reflect more broadly on global health: if the resources now being expended on a COVID-19 vaccine had been focused years ago on other infectious diseases like malaria (resulting in over 400.000 deaths per year globally), or mostly preventable diseases like lung cancer (at least 1,5 million deaths per year), the world would already be a long way to cures for these preventable diseases. The reasons these diseases do not appear as "global emergencies" are complex, but a large part is attributable to geography and demography. To be sure, the awkward juxtaposition of business interests and public health extends beyond rich, research-intensive countries and poor countries with public health emergencies. For example, research into cancer diagnostics languished for many years and is only being reinvigorated now that drug pipelines have dried up.

But rather than setting rules who can afford and cannot afford a vaccine, governments can use their power to be the purchaser. Despite objections in some quarters, one of the roles governments are best at is procurement and shipping. "Make a novel and widely useful antibiotic or vaccine and the government will compensate you properly" makes success more likely. The ongoing procurement coupled to a medically informed, equitable distribution of vaccines against the virus causing COVID-19 would be among the greatest contributions centralized government decisions have ever made to the health of humanity.

In a pandemic, each day matters for the health and life of tens of thousands of people. But this cannot be at the expense of safety or public acceptance. We worry for the safety of people in countries intent on pushing them through trials or onto the market without sufficient evidence for efficacy and safety. We hope that governments minimally will hold each other to standards for ethics, safety, medicine and for epidemiologically informed sharing, so that everyone can benefit from the invaluable work researchers are doing worldwide to control the COVID-19 pandemic. Early results from phase 3 trials offer hope for effective vaccines. To beat the pandemic we now need plans to get these effectively to the people.