



Racing against COVID-19

A long-term solution to COVID-19 includes vaccine development. Reinhilde Veugelers and Georg Zachmann propose a vaccines strategy for Europe to meet the challenge of future pandemics

The fast development of vaccines is an essential part of the long-term solution to COVID-19, but vaccine development has high costs and carries the risk of high failure rates. There are currently too few promising projects in the clinical trial pipeline to guarantee at least one vaccine soon. More projects need to pass through the development pipeline in parallel. Vaccines should ultimately be widely available to all who need them at low cost.

Private life sciences companies under-invest in vaccine development, especially when compulsory licensing and/or price regulations are imposed. Public funding is needed to reduce the risks of investing in vaccine development, and also to balance compulsory licensing and/or price regulations with incentives for private firms.

The public funding being put into identifying COVID-19 vaccines is too limited to carry enough projects through so that at least one vaccine, and preferably more, become available at large scale and low cost. Public budgets for these efforts need to be multiplied up several times over.

We propose a staged support scheme to tackle the COVID-19 vaccine challenge and a moon shot programme to meet the challenge of future pandemics. We calculate the public budget needed to ensure supply of COVID-19 vaccines. Although substantial, the budget represents a bargain compared to the avoided health, social and economic costs.

The COVID-19 vaccine challenge

To stop the COVID-19 pandemic, reopen the economy and prevent the pandemic from restarting, the world needs vaccines. Given how difficult and costly it is to engineer natural immunity, vaccines are critical for helping to build herd immunity to manage the disease.

But so far, no vaccines (or therapies¹) for COVID-19 have been approved by regulatory agencies. The genome of the virus was sequenced very quickly and put in the public domain, meaning that researchers were within a matter of weeks able to identify several promising vaccine candidates. Start-ups, legacy drug makers and research labs have stepped forward with plans to develop vaccines or treatments for COVID-19.

National and international public authorities have pledged funding for treatments and vaccines. There is much hope that a COVID-19 vaccine will be available soon – most optimistically in the next six months, though the most frequent prediction is 18 months².

The list of COVID-19 vaccine projects grows by the week, helped by the genetic code of the virus being made available very early on

But many questions remain. Are there enough projects in the pipeline to ensure a vaccine soon? Once successfully developed, can a vaccine be manufactured quickly on a large scale? Will it be available at a fair price? Can open access and fair prices be ensured without discouraging private developers? Who should fund the development and production costs?

We address these questions by examining success rates from previous vaccine-development projects and matching this, in terms of numbers of projects and funding, with what is currently in the pipeline for COVID-19. To ensure the successful development of COVID-19 vaccines in the European Union, we propose an EU publicly funded support scheme.

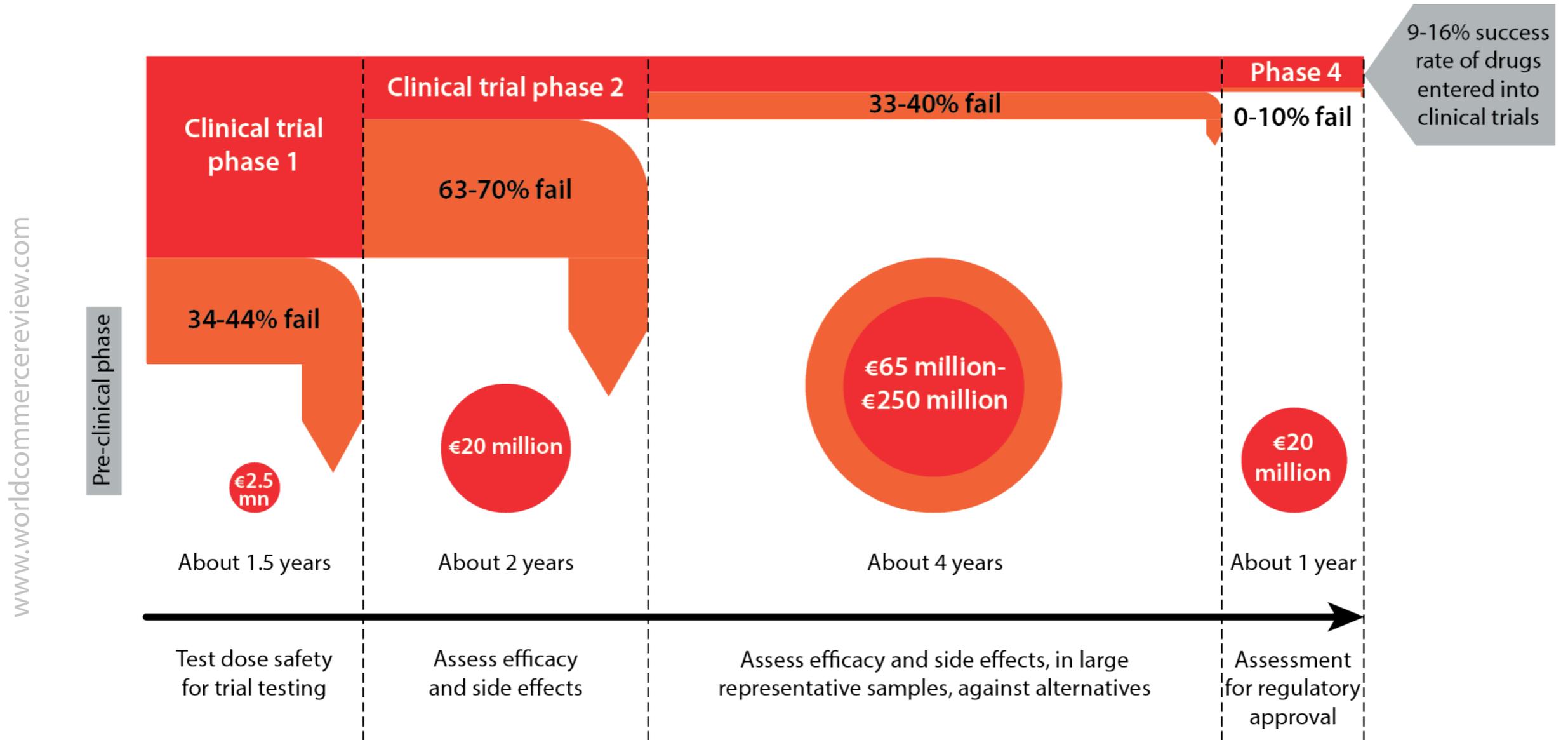
The long road to vaccine development

Drug development (for both treatments and vaccines) typically follows a clear path (Figure 1). At each stage, the development of a drug might be stopped for technical, medical or economic reasons. The different stages are characterised by different probabilities of success, and strongly varying costs and durations.

Figure 1 shows that the average success rate for drug development is about 10 percent to 15 percent. The high-risk rates imply that society needs many candidate substances at the outset of clinical trials to be sufficiently sure of getting a suitable product in the end.

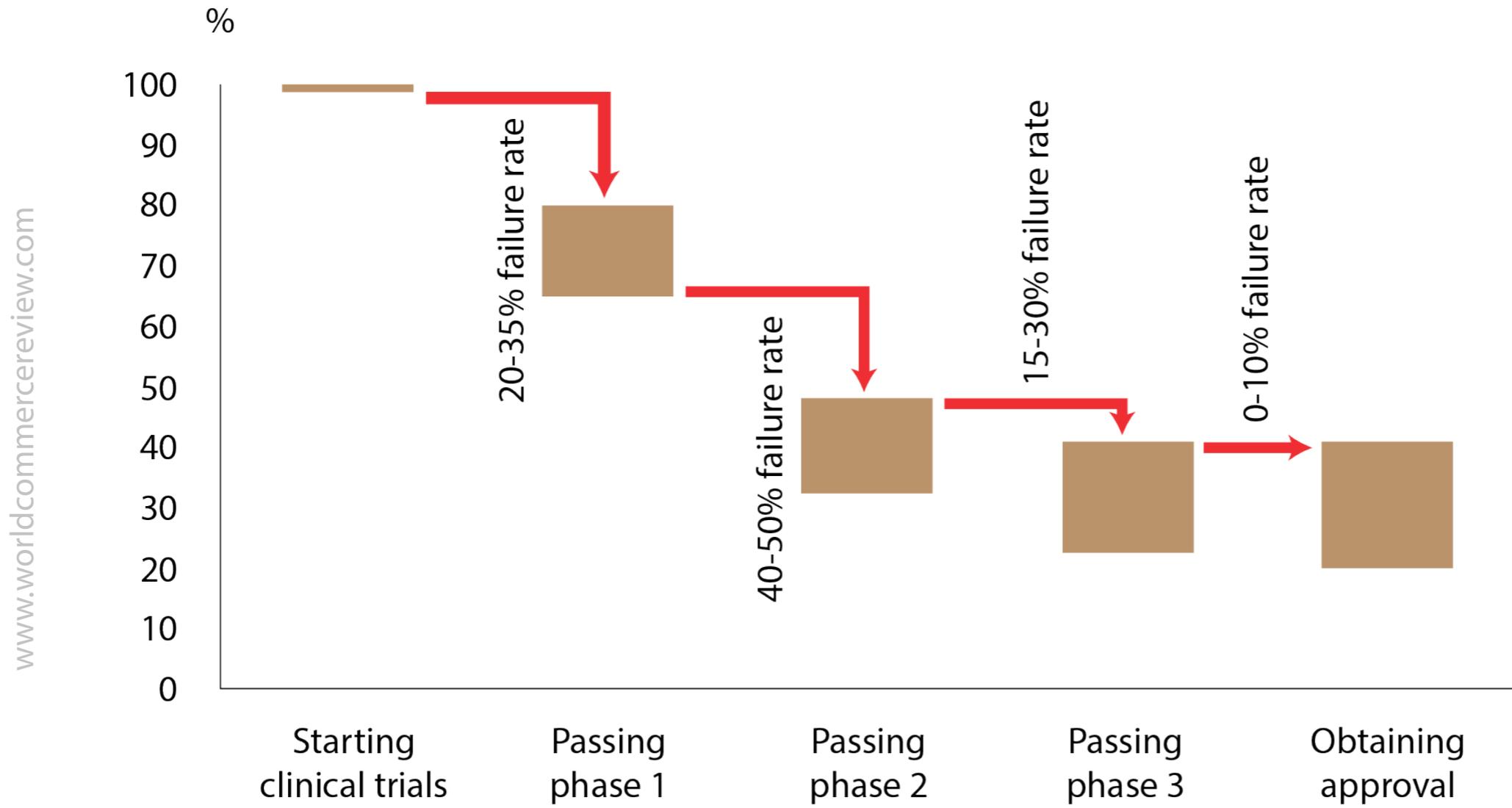
For vaccines, the success rates are higher than for medical drugs in general³. Success rates for vaccines that entered clinical trials can range from 20 percent to 40 percent (Figure 2). In particular, vaccines for new diseases, such as COVID-19, are more likely to pass the critical and expensive phase 3 because there are not yet benchmarks against which efficacy needs to be proved.

Figure 1. A typical trajectory of drug development⁴



Source: Bruegel. Note: Reported success rates are averages from six review studies, with the minimum and maximum values eliminated. For a list of the review studies, see the References. See also https://en.wikipedia.org/wiki/COVID-19_drug_development

Figure 2. Success rates for clinical trials of development for vaccines



Source: Bruegel based on review studies (see the References).

In addition, the time span for vaccine development can also be expected to be shorter than the average for drug development⁵. All regulatory authorities for medicines have fast-track procedures. Vaccines go through such fast tracking because they are typically developed in response to emergencies, often with no available benchmarks to prove efficiency against.

Also, agencies can authorise emergency use, allowing vaccines that are still in the process of clinical trials to be made available to some patients. This is however only for restricted exceptional cases, such as for medical personnel, and never on a large scale.

Repurposed substances – substances already approved for other diseases – can reuse past results and typically go much faster through clinical trials, with lower costs and higher success rates⁶.

Who develops vaccines?

Exploratory research and the pre-clinical and early stages of clinical trials can be done by researchers in research institutes or small firms. At later stages, however, particularly phase 3 and commercialisation, large life sciences firms typically take over.

They have the financial resources for these more expensive stages, experience of managing large clinical trials and regulatory approval procedures, and they have the commercialisation capability (manufacturing, distribution and marketing)⁷.

In the last few decades, the vaccine industry has been through a major consolidation, leaving only a handful of large life sciences firms active on the market. The largest life sciences companies for vaccine production (in terms

of vaccine revenues) are GSK, Merck, Sanofi and Pfizer (Statista, 2020). Johnson & Johnson, through its subsidiary Janssen Pharmaceutica, currently has the largest number of vaccine projects in preclinical trials (Statista, 2020).

How is vaccine development financed?

National and international public research money typically funds the initial exploratory research phase, often done by university labs or research organisations. Funders include the US National Institutes of Health, and the European Union through its multi-annual research programmes⁸. Philanthropists, such as the Bill & Melinda Gates Foundation, are prominent funders. Also, big life sciences companies provide some funding for vaccine research.

The vaccine development phases, typically done by private companies, are funded either by large life sciences firms themselves or through company partnerships. Their returns from investing in vaccine development depend on the exclusive ownership they can obtain of the right to use the ultimately approved substance or technology.

As ownership of knowledge and claims can be identified clearly in drug development, patents are very effective in protecting the intellectual property and ensuring exclusive ownership during the patent lifetime. Patents are used heavily in this industry.

Typically, platform technologies and mechanisms of action (how to treat a certain illness with a certain substance) are patented early on in the process. The owners of the patents for successful drugs/vaccines might be the original applicants, but developers can also acquire patent rights by buying or licensing from others during the development process.

External funding for development is available mostly through public-private partnerships. Particularly for the later more expensive clinical trial stages, public funding if provided at all, is through co-funding with private developers.

In the US, the public part of these partnerships is channelled through the Biomedical Advanced Research and Development Authority ([BARDA](#)). At the EU level this is channelled through the Innovative Medicines Initiative ([IMI](#)), a public-private partnership between the EU and the European Federation of Pharmaceutical Industries and Associations (EFPIA). Debt and equity funding for vaccines and other initiatives is also provided via the European Investment Bank's InnovFin Infectious Diseases Finance Facility (IDFF).

Another recent major funder of vaccine development is the global Coalition for Epidemic Preparedness Innovations (CEPI), set up in 2017 with a targeted \$1 billion fund. Its financing partners include the Gates Foundation and a number of countries. The EU, through IMI, is also a partner (<https://cepi.net>).

Specific challenges for COVID-19 vaccine projects

On top of the high overall failure rate of clinical trials of vaccines, COVID-19 poses specific challenges (*The Economist*, 2020).

First, there is no current close substitute vaccine available from other corona- or other viruses, which could be repurposed quickly for COVID-19. The 2003 outbreak of SARS (severe acute respiratory syndrome), also caused by a coronavirus, was controlled after four months, impeding the development of a vaccine. In hindsight, this was unfortunate, as a SARS vaccine could have helped to accelerate the development of a COVID-19 vaccine.

Another challenge is the scale at which the vaccine, when available, needs to be produced and made available throughout the world to provide herd immunity. A vaccine made for the world has never been done before. The Gates Foundation is already trying to address these large-scale manufacturing challenges by funding new factories for potential coronavirus vaccines⁹.

Nevertheless, existing technologies to develop and manufacture vaccines can be used as a platform for a COVID-19 vaccine. Some COVID-19 vaccine projects are based on proven approaches to vaccines, which use modified forms of the virus. The advantage of this approach is that it is well tested, with a stock of expertise, including for manufacturing. However, as it involves cultivating live cells, manufacturing cannot be quickly scaled up.

Other projects use newer approaches focusing on genetically engineered synthetic vaccines that activate the body's immune response. The active ingredient in these vaccines can be the virus's DNA or RNA (the genetic instructions for building proteins), or the proteins/spikes that let the virus enter into human cells.

These vaccines can be quickly developed, as scientists only need the virus's genetic code, which was made available very quickly for COVID-19. Such synthetic vaccines should in principle be faster and cheaper to manufacture at large scale. However, they face a higher risk of failure in clinical trials. There are no human DNA or RNA medicines on the market yet¹⁰.

Because each approach carries specific risks, a variety of approaches will be needed to get a successful vaccine for COVID-19 through development. Vaccines developed through different approaches might also be better suited to specific population subtypes.

The pipeline of COVID-19 vaccine projects

The World Health Organisation by March 2020 had identified more than 40 promising COVID-19 vaccine projects¹¹. CEPI by the end of March had identified 78 active projects (Thanh Le *et al*, 2020). The list grows by the week, helped by the genetic code of the virus being made available very early on. See the Appendix for more information on current vaccine development projects.

Almost all of the projects are, at time of writing, still exploratory or at the preclinical stage. The only projects to have started clinical trials (as recorded on the [ClinicalTrials.gov](https://www.clinicaltrials.gov) website) are Moderna and Inovio in the US and CanSino Biologics in Hong Kong. Two mainland Chinese projects have also started clinical trials¹².

All of these started clinical trials in March 2020 and have thus not yet produced results from tests on actual patients, which is when the major dropouts occur (Figures 1 and 2). Europe has several projects at the exploratory research or preclinical stages, but no projects in clinical trials at time of writing. The German project CureVac is probably the closest to starting clinical trials.

The projects cover various technological trajectories. Projects using the newer but riskier genetic engineering technologies are for the moment in the lead: Moderna and CureVac are using mRNA (Messenger RNA) technology and Inovio DNA technology in clinical trials. These approaches have a clear advantage in speed of development, but come at a greater risk of not getting a vaccine successfully through clinical trials, as DNA and mRNA synthetic engineering technologies have never been trialled successfully on humans.

Among the large life sciences companies, only Johnson & Johnson, Sanofi and Pfizer are actively involved in developing a COVID-19 vaccine, in partnership with small biotech or research organisations. GlaxoSmithKline (GSK) and Merck, each with substantial experience in vaccine development, are not yet directly involved, although GSK is providing its adjuvant 'booster' technology to other developers, including Pfizer.

Nevertheless, engagement in vaccine development by large life-science companies cannot be taken for granted. While research institutes stay mostly confined to the early research stages, small biotech firms are the typical lead developers for COVID-19.

The few trials at the time of writing are being carried out by companies that are small and/or inexperienced in phase 3 clinical trials and that lack large-scale vaccine manufacturing capability. In addition, as small biotech companies do not have deep pockets, external funding for the more expensive later development stages still needs to be secured.

Of the COVID-19 clinical trial projects underway, external funding for phase 1 has been secured by Moderna (from the US National Institutes of Health and CEPI) and Inovio (from CEPI and the Gates Foundation).

However, neither has yet secured funding for the most expensive later stages, nor secured large-scale manufacturing capacity. For the preclinical and exploratory research projects funding has been secured only for the early stages, if at all. All would have to seek partnerships with large life sciences companies, or with public and philanthropic funders.

The German CureVac project is a notable exception. It had the good fortune to secure a substantial amount of European public funding from the European Investment Fund to cover its total development costs. Johnson & Johnson has also secured enough funding for the whole pipeline, with the US Biomedical Advanced Research and Development Authority providing half of their funding. Box 1 provides an overview of what the EU is currently funding for COVID-19 vaccines.

Are there enough projects and funding in the pipeline for a COVID-19 vaccine soon?

Based on failure rates of past vaccine development projects (Figure 2), we can predict how many projects¹⁴ are needed at the start of the COVID-19 clinical trial pipeline, in order to have close to certain chance (say 99 percent) of at least one successful vaccine.

Box 1. EU COVID-19 vaccine funding

Prior to the COVID-19 pandemic, the EU already provided €500 million for vaccine and vaccination research through the Horizon 2020 research programme (2014-2020). It has also co-funded the development of vaccines through IMI (see section 2) and the European Investment Bank.

To respond to COVID-19, the EU has provided emergency funds to support research and development of diagnostics, therapeutics and vaccines. A rapid reaction has been made possible by the standing budget line for emergency health research that the Commission maintains as part of the Horizon 2020 annual work programmes.

- IMI in March 2020 started a fast-track call for projects on development of coronavirus therapeutics and diagnostics. Preventive vaccines were explicitly excluded from this call. The EU provided €45 million for this call, with the same amount expected to be provided by the private partners in IMI.
- Initially €10 million, subsequently increased to €47.5 million, was provided for research projects to respond to the COVID-19 pandemic. Of the 18 research projects short-listed for funding in March 2020, two were for a potential vaccine:
 - €3M for Sweden's Karolinska Institutet. Its project will start animal testing soon, with first trials on humans expected to begin in 2021 (<https://news.ki.se/vaccine-development-against-coronavirus-enters-next-phase>).

- €2.7M for a consortium led by Denmark's AdaptVac, for the development and clinical testing of a novel vaccine. The company said it aims for the vaccine to complete initial human clinical testing within 12 months (<https://www.adaptvac.com/news>).

- The March 2020 round of the European Innovation Council Accelerator call, with a budget of €164 million, includes a fast-track for coronavirus relevant proposals; see https://ec.europa.eu/info/news/startups-and-smes-innovative-solutions-welcome-2020-mar-13_en
- The European Institute of Technology Health opened in April 2020 a call to EIT partners to send proposals for COVID-19 projects with rapid implementation. EIT Health will fund each project with up to €600,000. Vaccine and drug development are not supported under this call. See <https://eit.europa.eu/our-activities/opportunities/apply-now-eit-health-covid-19-support>

CEPI funding and the EU contribution to CEPI

In January 2020, CEPI (Coalition for Epidemic Preparedness Innovations) announced the start of programmes to develop COVID-19 vaccines. On 6 March, CEPI **called** for \$2 billion in additional funding these programmes¹³. CEPI's total investment in COVID-19 vaccine R&D, at time of writing, is \$29.2 million. The EU has contributed to CEPI via Horizon 2020.

If there is a probability of between 20 percent (pessimistic scenario) and 40 percent (optimistic scenario) that COVID-19 vaccine projects that start clinical trials will reach the final stage (Figure 1), between nine projects (optimistic scenario) and 21 projects (pessimistic scenario) are needed. With only two COVID-19 vaccine projects having started clinical trials in the US so far – five when including the Chinese projects – it is not yet sure there will be at least one vaccine at the end, even in an optimistic scenario¹⁵.

If the cost of the various clinical stages are similar to the costs for drugs in general¹⁶, then the costs covering the full development of a vaccine associated with a 99 percent probability of success will be from €500 million in the optimistic scenario of needing only nine projects starting clinical trials to around €2 billion in the pessimistic scenario in which 21 projects are needed.

These amounts would cover only clinical development and regulatory approval, and not the early research and preclinical trial phases. Costs of production and supply of the vaccine are also excluded.

However, it is not a winner-takes-all race in a search for one successful vaccine. Different vaccines might be needed. Multiple pathways to a vaccine are important, as this will help to reduce the risks. Multiple vaccines might also address the large-scale production challenge and will prevent monopoly bargaining positions at the end of the pipeline, which would impede large-scale availability at low prices. Multiple vaccines would also be better address differences in effectiveness in view of differences in immunity or tolerance for different groups of the population.

If enough substances are brought forward to enable success with a probability of 99 percent, statistically there will be on average four successful projects. To be 99 percent sure of getting at least three different success cases¹⁷, about 20 projects should start clinical trials in an optimistic scenario (taking the upper bound of success

probabilities), and 40 projects should start clinical trials in a pessimistic scenario (taken the lower bound of success probabilities). This would increase the cost range to around €725 million (optimistic) to €3 billion (pessimistic).

The need for public support

The social value of a universally accessible COVID-19 vaccine is huge. The health, human and economic cost of COVID-19, which would be avoided if there was a vaccine, is difficult to appreciate. Even if only early estimates are considered of a global loss of GDP of 6 percent in 2020 (IMF, 2020) from COVID-19, the cost would be about \$5 trillion.

Compared to what is socially desirable, private companies are likely to underinvest or invest too slowly in the development of a COVID-19 vaccine. Private companies and their investors, when deciding to engage in COVID-19 projects, will balance the development costs and risks against the returns they expect, making comparisons to alternative possible projects.

Companies can decide to shift developers from other, commercially more promising, work to COVID-19 or vice versa. If private life sciences companies do not believe governments will allow them to charge high enough prices for a vaccine, in order to recover the costs and risk of development, they will only work with limited resources or not at all on the development of a vaccine for COVID-19, preferring to focus on other more profitable development projects.

Fully focusing their expertise and attention on COVID-19 requires a proper balancing between government intervention and incentives for private firms. Yet, the private business case for vaccine development is not straightforward, explaining why the share of private R&D expenditure on vaccines compared to other drugs is small¹⁸.

Private developers and private funders will want to be compensated by the expected returns on vaccine sales in case of success, but vaccines, compared to other drugs, might carry greater commercial risks. Vaccines for highly communicable diseases with serious negative health effects, such as COVID-19, need to be made widely available to all in need.

This makes the potential market for these vaccines huge, and would generate the reputational gain from giving the world a COVID-19 vaccine it so desperately needs, but these returns on a COVID-19 vaccine might not be sufficiently interesting for private drug companies, compared to the high cost and risk, and compared to alternative projects.

There are several reasons why the private profits to be made from developing a COVID-19 vaccine will be drastically below the vaccine's social value:

- Patients will be much more willing to pay for drugs that help them directly, than for vaccines that help them in case of an outbreak, and which have positive immunity effects against others.
- These externalities imply that vaccines for highly communicable diseases such as COVID-19 cannot simply be sold to the highest bidders. These vaccines should be available on the basis of social needs, not individual willingness and capacity to pay. Generating herd immunity to eradicate the pandemic requires access to vaccines for all social classes in rich and poor countries and this would require fairly low prices.

For these reasons, COVID-19 vaccines are more likely to be purchased by government agencies and at low prices. Commercial developers must worry that they cannot negotiate prices freely with governments, increasing the commercial risks.

- Finally, the existence of front-runners in COVID-19 vaccine development represents a commercial risk to other developers. It implies a significant uncertainty over the size of the market.

With private returns drastically below the COVID-19 vaccine's social value, public intervention is needed to ensure that a socially-sufficient number of vaccine projects are under development at a socially-sufficient speed. Public intervention is also needed to have vaccines being manufactured and distributed to all that need them and soon (Blanchard, 2020).

This public intervention can take the form of public funding of development, funding or provision of manufacturing facilities, conditions on access to the proprietary technology of the successful vaccines through compulsory licensing, and/or controls on the prices of the vaccines.

Some countries have already said they will look into compulsory licences for COVID-19 vaccines¹⁹. The problem with these interventions is that they need to be balanced against the incentives for private developers. For this reason, public de-risking of vaccine development and fair access should go hand-in-hand.

An additional concern with public intervention is that individual countries might have an incentive to under-invest in public support for a COVID-19 vaccine compared to what is globally socially optimal.

Individual countries might bet on acquiring foreign solutions when they become available, instead of spending their own financial, medical and research resources. The countries that are able to provide finance should collaborate, with a commitment to supply the successful vaccines to all countries in need.

Our proposal

Although the pipeline of COVID-19 vaccine projects at the exploratory and preclinical stages is substantial, and there are public funding initiatives, more projects are needed and more public money than currently should be put into getting them through clinical trials.

Based on past clinical trial success rates, we calculated that at least nine projects starting clinical trials are needed (to have a 99 percent probability of at least one vaccine, using the upper bound of success rates). Ideally, more projects are needed to ensure multiple vaccines.

The current public funding we have been able to identify is too limited to enable a sufficient number of competing projects, in order to be sufficiently sure that vaccines can be available quickly. Missing in particular is a commitment to public funding of projects through their later, more-expensive stages of development.

With a few exceptions (including CureVac, Johnson & Johnson and Sanofi-GSK), and disregarding for now the Chinese projects, typically backed by the Chinese state, none of the preclinical projects have secured funding for the later stages of development, should they succeed in their early phases.

Although Europe has projects in the pipeline, it has no projects yet in clinical trials. Most European projects are not assured yet of public funding for the later, more expensive stages of development. As it stands currently, European citizens cannot be sure they will be likely to have affordable access to a vaccine soon, particularly if vaccines successfully developed in the US or China face export restrictions, even though the EU and its members are willing to increase funding for the development of COVID-19 vaccines²⁰.

To address the possible shortfall, an EU funding scheme should be put in place to increase the number and speed of projects to get a COVID-19 vaccine through clinical trials. The scheme would involve a series of awards or grants, organised as an open continuous call until the critical number of projects is reached.

The aim would be to identify at least three suitable vaccines at the end of the pipeline, with more than 99 percent probability. Public funding would cover the costs of each phase and would be conditional on projects starting the phase. Table 1 sets out the scheme of awards.

Project proposers at each stage would have to agree when receiving an award that on final success, the patented technology will be made freely available for manufacturing. This compulsory licensing would be balanced by the full public funding of the development costs, thus not jeopardising the incentives for private applicants to engage in development of a COVID-19 vaccine.

The total budget required for the scheme would range from €725 million in an optimistic scenario to about €3 billion in a pessimistic scenario. The total is driven up by the projects in phase 3, representing 80 percent of the total budget in the pessimistic scenario, or somewhat more than half in the optimistic scenario. Even though the staging of the scheme would help reduce the risks, the required budgets are nevertheless substantial and above what could typically be done within the EU budget.

One way to raise the amount of money to finance the scheme would be to build on the idea of corona or recovery bonds, which could use the EU budget as a financial vehicle to borrow funds on the market and leverage them for large-scale investments.

Table 1. COVID-19 vaccines public funding scheme

Numbers and amounts of awards needed for each stage to ensure that at least three vaccines complete all clinical phases, under optimistic and pessimistic assumptions

Optimistic scenario (high success probabilities, low cost estimates)				
	Assumed success rate	Size of the award	No. awards at this stage	Total cost of awards
Phase 1	40%	€2.5 million	18	€45 million
Phase 2	51%	€20 million	13	€260 million
Phase 3	85%	€65 million	6	€390 million
Approval phase	100%	€10 million	3	€30 million
Pessimistic scenario (low success probabilities, high cost estimates)				
Phase 1	20%	€2.5 million	40	€100 million
Phase 2	32%	€20 million	25	€500 million
Phase 3	63%	€250 million	10	€2,500 million
Approval phase	90%	€10 million	5	€50 million

Source: Bruegel (see Figure 2)

The EU would not have to be the sole funder. With a pledging event, it could collect a pool of money from public and philanthropic donors. But the EU should use its capacity to take the lead in setting up the financing, by pledging a substantial share of the total amount required.

It would be a valuable signal if the EU would already today commit to providing funds, even if the detailed rules are only spelled out tomorrow. To save time, the organisation of the scheme should be done by an agency with a track record in organising funding schemes for vaccine development. IMI comes to mind, particularly if it can collaborate closely with the European Investment Fund and particularly with CEPI, in which it is already a partner.

Why would such a scheme be needed, compared to what the EU is already doing?

- Compared to the normal pipeline of projects funded by the European Commission, a focus on development rather than research is needed, and not only on the initial stages, but through to the end of the pipeline. This requires bigger than normal public funding.
- The division into different phases would mean the bigger amounts only need to be activated for those projects that reach the more expensive later phases. Staging would avoid the need to commit large funds upfront.
- Under our proposal, contenders would be sure from the start that there is a scheme available for funding all stages in case of success, including the more expensive later stages. Some projects might have been able to secure full funding from private sources, but only those with a high enough probability of being first. Full funding from private sources cannot be assured for all the projects that are needed by society at the start, in order to generate multiple successful vaccines.

- The scheme would be run as an open, continuous call, not with fixed call deadlines, and with awards given out in parallel rather than serially. Offering the awards in parallel would reduce the overall timeline. The same applicants can also apply simultaneously to the various calls with multiple projects at different phases.
- Our proposal does not back one winner initially, nor does it bet on one winner at the end. It is calibrated to ensure multiple successful projects at the end. Supporting multiple projects at the start would reduce the high risk of clinical trial failures and ensure at least three vaccines.
- The compulsory licensing condition will mean vaccines become available for production and distribution at competitive market rates. This compulsory licensing is a clear condition ex ante in return for the full public funding of the development costs.

It should therefore not reduce the incentives for applicants to engage in a COVID-19 vaccine project. It also lessens the commercial uncertainty surrounding the use ex post of compulsory licensing for COVID-19 by at least some countries, which might deter private companies from engaging in the development of a COVID-19 vaccine.

For COVID-19, it is critical that vaccines should be available at large scale and low cost. Our scheme does not include public support for the manufacturing and distribution of the successful vaccines. However, it does contribute to addressing this critical challenge.

- Ensuring multiple vaccines at the end, combined with compulsory licensing, will lead to a competitive supply of vaccines at no/low licensing cost, avoiding supply restrictions and marked-up prices from firms with market power.

The scheme thus avoids the need for public funding ex post to provide subsidies so vaccines can be bought by all who need it. It also avoids having to deal with the complexity of designing a socially optimal subsidy scheme, to match willingness to pay with needs, and to deal with problems of segmenting markets and parallel imports. It should also remove the incentives for private big pharmaceuticals firms to go it alone, in the hope of being the first to win the market in search of monopoly rents.

- In addition, the organising agency can set up a taskforce dedicated to finding the capacity and funding for manufacturing at large scale for the successful candidates. It can do this from the start of the scheme to save time, even when it is not yet clear which projects will be successful²¹.
- The agency could also plan the optimal distribution of the vaccines to where they are needed most within the EU.

Although the scheme would be an EU initiative activating EU funds to ensure that EU citizens have quick access to COVID-19 vaccines, the initiative should not become a 'fortress Europe'.

- The agency running the scheme should seek out international collaboration with other similar initiatives. Having a significant European instrument might provide leverage in ex-ante negotiations of international cross-licensing agreements (with the US or China).

An agreement to cross-license final vaccine technologies would reduce the number of projects needed under each programme, reducing the financial burden. Such negotiations are easier to do ex ante than after one of the partners has already found a vaccine.

- This agency could also coordinate with the appropriate organisations, such as the World Health Organisation, to allocate the vaccines worldwide to where they are needed most.
- The EU would have with this scheme a tool to provide the compulsory licensing terms for the successful vaccines it generates, not only within the EU but also to all those around the world who need it. The initiative would thus show the EU as a beacon in dark times when leadership is critically needed to organise global coordination and deal with the COVID-19 pandemic.

In addition to this series of awards to address COVID-19, we call for a moon shot programme in order to be better prepared for the next pandemic. This would support research into new and faster approaches to vaccine development, universal vaccines and broad platforms for vaccine development.

This programme can involve a normal grant competition. It could be done within the regular EU framework programme, but would be best done with international coordination, for example with CEPI or the Gates Foundation, which in summer 2018 (together with Larry Page) launched a \$12 million fund for universal vaccine projects. One could easily imagine a budget of double that for an EU moon shot at 'vaccines for the future' ■

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Endnotes

1. This contribution focuses on the economics of the development of vaccines, but many parts of the analysis would also apply to treatments for COVID-19. Vaccines and treatments are anyway complementary (see Eichenbaum et al, 2020).

2. "Dr. Anthony Fauci, the head of the National Institute of Allergy and Infectious Diseases (NIAID), poured cold water on Trump's estimate, saying it would be more like a year to a year and a half." See <https://edition.cnn.com/2020/03/31/us/coronavirus-vaccine-timetable-concerns-experts-invs/index.html>
3. Fewer studies look at the success rates by type and phase, leading to less-robust estimates of success rates for vaccines at the different clinical trial stages. An extreme example is a study by Pronker et al (2013), quoted by Gouglas et al (2018), who reported: "In general, vaccine development from discovery to licensure can cost billions of dollars, can take over 10 years to complete, and has an average 94% chance of failure." The success rates we have used are based on a large set of studies, with the lowest and highest extremes eliminated.
4. The research phase before the pre-clinical and clinical development phase is not considered here. This exploratory phase may take many years and involve many dead ends. Also not included are production and commercialisation. The costs of the production and commercialisation stages vary widely.
5. For instance, it took just ten months for the vaccine for Ebola to go from phase 1 to phase 3 trials (The Economist, 2020).
6. Hydroxychloroquine, used to treat malaria, is an example seen by many as a potential treatment for COVID-19. It has not been fully trialled as a COVID-19 treatment.
7. As an exception, a clinical trial for treatments for COVID-19, planned to involve 3,200 patients in eight European countries with severe COVID-19 infections, was started in March 2020 by the French national health research agency Inserm. This example shows that even phase 3 can be done without big pharmaceutical companies, and can be done with international coordination.
8. For a list of EU-funded research projects on vaccines, relevant for COVID-19, see <https://erc.europa.eu/news-events/magazine/frontier-research-service-coronavirus-epidemic-response>
9. This is being done though the money could be wasted if vaccines are not developed. See Brianna Moné, 'Bill Gates is funding new factories for 7 potential coronavirus vaccines, even though it will waste billions of dollars', Business Insider, 3 April 2020, available at <https://www.businessinsider.nl/bill-gates-factories-7-different-vaccines-to-fight-coronavirus-2020-4/>

10. For a more detailed description of the various approaches, see, for example, Cohen (2020), Thanh Le et al (2020) and The Economist (2020).

11. See https://www.who.int/blueprint/priority-diseases/key-action/Novel_Coronavirus_Landscape_nCoV_Mar26.PDF?ua=1. The WHO is not directly funding projects, but is involved as coordinating international exchange of information, developing and sharing common blueprints, and international cooperation to accelerate diagnostics, therapies and vaccines.

12. The two Chinese projects are from Shenzhen Geno-Immune Medical Institute, a very recently established institute, funded by the Shenzhen government. There is no information available on their COVID-19 vaccine projects on the WHO site, nor on the Institute's English website. In addition, Xinhua reported on 14 April 2020, the start of two more COVID-19 vaccine clinical trials in China, but neither is reported on [ClinicalTrials.gov](https://clinicaltrials.gov). One of these trials is from Sinovac (see the Appendix), and the other is from the Wuhan Institute of Biological Products, a subsidiary of state owned SinoPharm.

13. See https://cepi.net/news_cepi/2-billion-required-to-develop-a-vaccine-against-the-covid-19-virus-2/

14. This section is focusing on the likelihood of securing vaccines. In terms of how long it will take for vaccines to be available, we are aligning on the most frequent prediction of about 18 months.

15. The number of projects needed increases non-linearly with required success rates. In other words, getting in the optimistic scenario to an 80 percent success probability would require only three projects compared to the nine projects required for a 99 percent success rate. Five projects would already give a 93 percent success rate. We believe that in the case of COVID-19, society cannot afford a probability that is not as close as possible to certainty.

16. As we don't have reliable estimates of the costs of vaccine-development projects, we use the numbers from general drug development reported in Figure 1: €2.5 million for phase 1; €20 million for phase 2, €65-250 million for phase 3 and €10 million for approval.

17. CEPI's ideal scenario is to have funding for three successful projects at the end of the pipeline: https://cepi.net/news_cepi/2-billion-required-to-develop-a-vaccine-against-the-covid-19-virus-2/

18. Established pharma companies only devote about 5 percent of their total R&D expenditures on vaccines. See CCVI (1993).

19. Germany, Canada, Australia and Chile have all taken steps or are weighing up moves to issue compulsory licences more easily. AbbVie gave up its global intellectual property rights for Kaletra, an HIV drug being assessed as a COVID-19 treatment, after Israel issued a compulsory licence that enables the country to use it against coronavirus without the patent holder's consent. See Donato Paolo Mancini and Hannah Kuchler, 'AbbVie drops patent rights for Kaletra antiviral treatment', *Financial Times*, 23 March 2020, available at <https://www.ft.com/content/5a7a9658-6d1f-11ea-89df-41bea055720b>

20 European Commission president Ursula von der Leyen said on 15 April she would host an "online pledging conference" on 4 May 2020. See https://ec.europa.eu/commission/presscorner/detail/en/STATEMENT_20_664

21. As the Gates Foundation is doing; see footnote 9.

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This article is based on Bruegel Policy Contribution 07/2020, Veugelers, R and G Zachmann (2020) '[Racing against COVID-19: a vaccines strategy for Europe](#)'.