The vaccine ecosystem and why it requires reform

Science has the potential to solve many of the world's most significant infectious disease threats through creating new vaccines. However, without significant change and reform of the ecosystem which drives vaccine and broader pharmaceutical development, the likelihood is that the world will not see these new vaccines come to fruition.

Potential new vaccines need to navigate complex and difficult processes to get through to reach roll-out. These include Research and Development (R&D), manufacturing, regulatory approval, and market entry. All of this takes time and costs money: over 10 years and on average US$500m. It is also a risky endeavour: fewer than 4 out of 10 vaccine candidates successfully make it through development. For some vaccines, the market works. If a vaccine is likely to make money without costing too much or carrying too much risk of failure, it will attract investment – in fact, it has probably already been developed.

For other vaccines, it's not so easy. Several types of vaccines face particular difficulties:

- Vaccines against diseases which cause outbreaks, epidemics or potentially pandemics, like Ebola or MERS-CoV (a coronavirus related to the virus which causes Covid-19). We don't know whether or when outbreaks might happen, so there is no predictable demand or market for these vaccines.

- Vaccines against diseases predominantly found in lower-income settings, like shigella (which kills over a million people every year, mostly young children). Since these diseases don't affect high income countries, the market and profitability for them is small.

- Vaccines against diseases which are relevant for antimicrobial resistance (AMR), like Group A Streptococcus. As there are currently effective antibiotics for treating these, the full value of vaccination against these pathogens is often underappreciated, leading to uncertain demand and disincentivising investment.

The world needs vaccines for the many escalating disease threats which do not have commercial markets. There are viable vaccine candidates waiting in the pipeline which have immense potential to save and improve lives in low and middle-income countries.

In late 2019 The Wellcome Trust commissioned MM Global Health to analyse the vaccine development ecosystem and identify the pivotal barriers affecting vaccine candidates in their journey to licensure and use. The analysis focused on vaccines for three types of diseases: those with epidemic or outbreak potential, those affecting low-income settings and those related to tackling antimicrobial resistance. The research included a full literature review, detailed mapping of vaccine development decision making, weighting of barriers in the ecosystem and analysis of existing solutions. The research provides a framework for understanding the potential improvements and actions which could be taken with respect to the vaccine market and ecosystem going forward.

Overview of the research

Understanding vaccine decision making

Decisions on whether vaccines progress are taken by those organisations directly involved in vaccine development, from academic institutions through to major pharmaceuticals. Other stakeholders such as regulators, funders, governments, and multilateral institutions all play a role in influencing whether a vaccine candidate will progress, but do not hold any final say on whether this happens.

Early decision making in vaccine development is generally undertaken by different sets of actors to those who make late-stage decisions. Academic institutions and biotech companies involved in early-stage vaccine development tend to focus more on unmet medical need and the technical feasibility of vaccine development. As a vaccine candidate progresses, a large-scale partner will be required to seek licensure and commercialisation. As larger, more commercial entities become involved, decision making around whether vaccines progress or not, shifts towards their value creation and revenue potential. Operating across the whole process is the issue of licensure feasibility. The lack of a regulatory route for a vaccine to receive approval is a key consideration for all stakeholders.

A complex system with interlinked challenges

The research identified 54 challenges faced by developers in advancing vaccines. These challenges were further explored through a survey of developers and via a series of role-played investment decisions involving an expert advisory panel. Of the 54 challenges 16 were found to be universal across the vaccine development ecosystem. Values for the cost, time and public health impact of addressing these barriers were calculated by bringing together the best available data and expert insight.

The report identified priority challenges which cut across regulating vaccine development, how we conduct clinical trials going forward, how we manufacture vaccines and how we finance vaccines that lack clear commercial markets. The challenges span science, industrial development, collective action, economics, and political economy. The challenges are also inter-related in nature with critical dependencies between the advances that can be made on scientific or technical barriers, and the advances required to provide sufficient economic reward to incentivise developers.

To date, efforts to solve the challenges in late-stage vaccine development have been singular approaches that have produced benefits for a single disease or single topic area but have not produced system-wide gains. Instead, a collective and systemic approach is needed, only then can the vaccine ecosystem be effectively equipped to meet the challenges of future infectious disease threats.

Why now?

Vaccine development for Covid-19 has shown us what *is* possible when you put everything behind getting the solution. The rules of the game were temporarily suspended: trials were run differently, regulators worked flexibly, and fast, political interest could not have been higher. But above all the money flowed and flowed fast, with payments made for vaccines which had not yet been created.

But if Covid-19 vaccines show us what happens when there is a global impact and therefore a clear commercial market for a vaccine, we only need to look to tuberculosis (TB) to see what happens when there is not one. Every year 1.4 million lives are lost to TB[1] and yet it has been over 100 years since any vaccines were licensed for use against the disease.

The research highlights the pressing need to create a sustainable vaccine ecosystem that supports us to solve all major infectious disease threats, not just those that affect high income countries.

What needs to happen?

- A systemic approach is needed to ensure the future vaccine ecosystem can meet all infectious disease threats.
- The use of innovative clinical trial models to promote more effective and less costly trials should be better enabled.
- Regulatory capacity must be increased to enable a range of improvements in how vaccines are developed and licensed.
- Efforts to build more global manufacturing capacity should consider how to ensure innovative and diverse approaches to mitigate the high costs and difficulty faced by vaccine developers.
- A radical rethink of the conventional models for the financing of vaccines will be required to address the pivotal barrier of the opportunity cost of investment in vaccines.

[1] WHO. (2020, October 14). Tuberculosis Factsheet. World Health Organization. Retrieved October 11, 2021, from https://www.who.int/news-room/fact-sheets/detail/tuberculosis