

# Virology

A therapeutic science transformed by biotechnology





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# What is a Virus?

A virus is a tiny, infectious particle that can reproduce only by infecting a host cell. Viruses "commandeer" the host cell and use its resources to make more viruses: "reprogramming" it to become a virus factory. Because they can't reproduce by themselves, viruses are not considered living. Neither do viruses have cells. They're much smaller than the cells of living things and are essentially just little packages of nucleic acid and proteins.

However, viruses do share some important features with cell-based life. For example, they have nucleic acid genomes based on the same kind of genetic code that is used in human cells and the cells of all living creatures. And just like cell-based life, viruses undergo genetic variation and can therefore evolve.

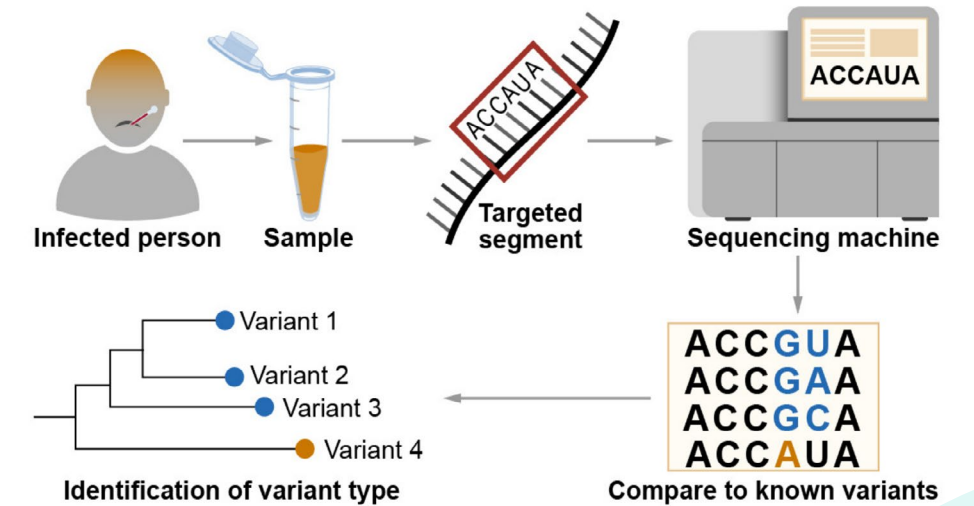
All viruses have genetic material made of nucleic acid. Cell-based life use DNA as their genetic material. Viruses can use either RNA or DNA. Today, DNA sequencing is used to identify and track the evolution of viruses. This has been evident to the public over the last two years with the tracking of the lettered "variants of concern" for COVID-19 with their different infectivities and severities.<sup>1</sup>

Viruses have receptors that allow them to attach to healthy (host) cells in the body. Once a virus attaches to and then enters a host cell, it can replicate (that is, make copies of itself). The host cell will die and then the virus can infect other healthy cells.



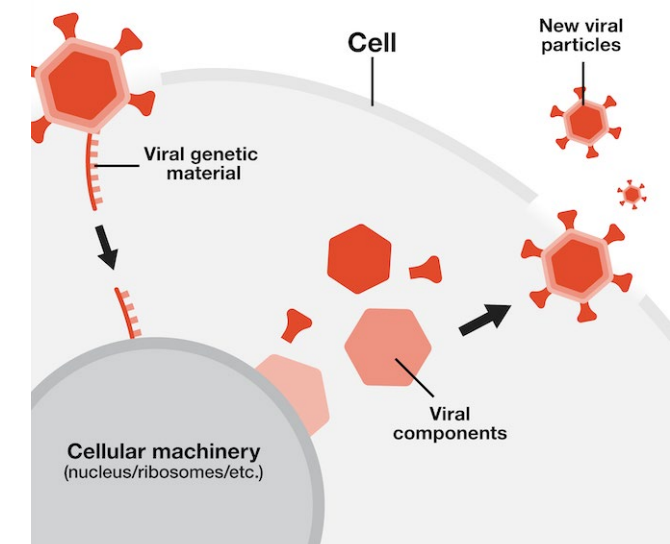
## Exhibit 1: Use of genomic sequencing in the identification of infectious pathogen variants. A, C, G, and U represent letters of the genetic code

Source: GAO-21-426SP, Science & Tech Spotlight: Genomic Sequencing of Infectious Pathogens



## Exhibit 2: How do viruses infect living organisms

Source: National Human Genome Research Institute: Genomics and Virology (genome.gov)



<sup>1</sup> See, for example, [Tracking SARS-CoV-2 variants - WHO](#) or [COG-UK and the sequencing of COVID-19](#)

# What is Virology?

Virology is the biology of viruses, virus-like agents and the associated diseases. It's a branch of microbiology that encompasses the structure of viruses, their classification and how they evolve. It includes the ways they infect and exploit host cells for reproduction, as well as their interactions with a host's physiology and immune systems. It also includes the diseases they cause, the techniques used to study them and the use of viruses in research and in therapies.<sup>2</sup>

<sup>2</sup> <https://www.niaid.nih.gov/diseases-conditions> and <https://www.nature.com/subjects/virology>



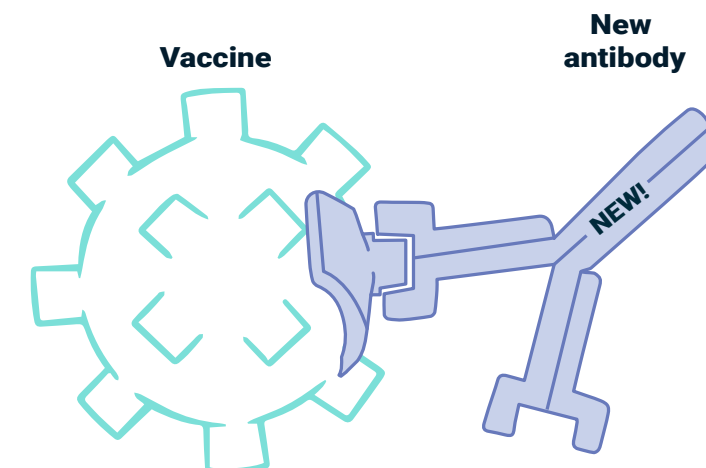
# What are Vaccines and Anti-Virals?

Anti-infectives is a general term used to describe any medicine that can inhibit the spread of an infectious organism or can kill the infectious organism outright. This term encompasses drug classes including anti-bacterials, anti-fungals, anti-parasitics, anti-virals and vaccines.

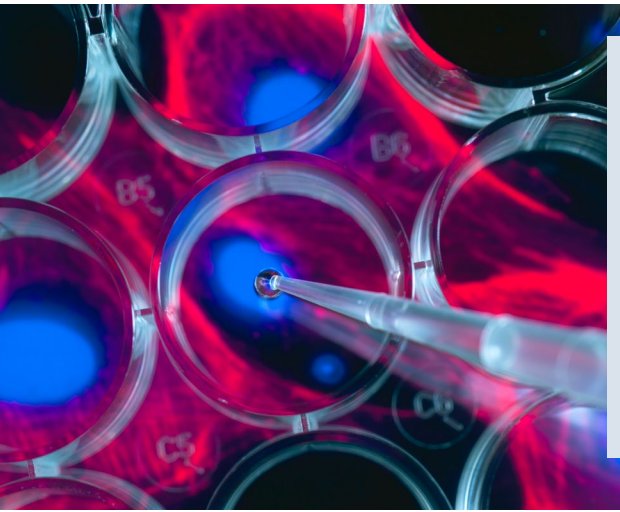
**Vaccines** are preparations used to prevent or mitigate the risk of infections. They are designed to induce a protective immune response in the body against, say, the virus represented in the vaccine. Once vaccinated, the immune system of the body produces a tailored response, consisting of specific T cells and specific antibodies that can help fight off the infection when exposure to the live virus occurs at a later stage. More importantly, vaccination also leads to the creation of a specific immunological "memory" against the viruses that each one is attempting to prevent. Upon contact with the virus at a later stage, the immune system can mount a specific response much more rapidly than an immune system of a person that hasn't been "primed" in the same way.

**Exhibit 3:**  
**Vaccines teach the immune system how to recognize pathogens, helping to fend off future infections**

Source: World Health Organization







It's been estimated that, ballpark, there exist 10 to the 31st power individual viruses on our planet!<sup>3</sup> Arguably, this makes viruses the most abundant "life" form on Earth. Human beings only manage to live in this virus-filled world, relatively free of illness, because these pathogens are very picky about the cells they infect, and only the tiniest fraction of them pose any threat. Of course, when they do, the impact can be quite terrible: from the plague of Justinian (a bubonic plague which killed half of Europe from 541 to 700) to the Black Death (which killed more than 75 million in Eurasia in the second half of the 14<sup>th</sup> century). Smallpox has been estimated to have killed 300-500 million in the 20th century alone until its eradication by vaccination.<sup>4</sup> The Spanish Flu infected a third of the global population in two years and likely caused 50 million deaths<sup>5</sup> while the HIV/AIDS virus and COVID-19 are two of the present viral risks.<sup>6</sup>

Of course, many common viruses now have vaccines available that help prevent or mitigate the disease that each causes.<sup>7</sup> Diseases caused by viruses including Measles, Hepatitis A and B, Diphtheria, Polio, and Chicken Pox have effective vaccines, often given during childhood, with lifelong efficacy. In fact, fatal or highly debilitating infectious diseases including Smallpox, Rinderpest, Polio, Measles, Mumps, Rubella and Cysticercosis have been or could be eradicated thanks to effective vaccinations.

Sadly, viruses without vaccines (and with for that matter) still cause death and debilitation worldwide. Communicable diseases including Chagas disease, Cytomegalovirus, HIV/AIDS, Hookworm infection and Leishmaniasis continue to be responsible for deaths around the world accounting for an estimated 26% of deaths globally in 2019.<sup>8</sup>

**Anti-virals** are drugs that can help treat people who have already been infected by a virus to reduce the severity of symptoms or the length of the infection. They also can be used to prevent or limit infection when given before or shortly after exposure but before illness occurs.

A key difference compared with vaccines is that current antiviral drugs are effective only when administered within a certain time frame before or after exposure and are effective during the time that the drug is being administered. Unlike vaccines that can prevent infection, antivirals act as a second line of defence, slowing down and eventually arresting progression of a disease when an infection occurs. They are also important when effective vaccines aren't available against viral diseases, for example for HIV, hepatitis C and herpes. Anti-biotics, another class of medicine, interfere with the reproduction of bacteria and are only useful for treating bacterial infections, not viral infections.

Viruses that do not resolve themselves may also require antiviral medications. Chronic or life-threatening viral infections, including COVID-19, Ebola, influenza, genital herpes, hepatitis B and C, and HIV, can all be treated with anti-viral medications. These block receptors so that the viruses cannot bind to and enter healthy cells, boost the immune system to help fight off the infection and overall lower the viral load in the body.

5 The Deadliest Flu: The Complete Story of the Discovery and Reconstruction of the 1918 Pandemic Virus | Pandemic Influenza (Flu) | CDC

6 <https://www.visualcapitalist.com/history-of-pandemics-deadliest/>

7 <https://www.who.int/news-room/questions-and-answers/item/vaccines-and-immunization-what-is-vaccination>

8 Global health estimates: Leading causes of death (who.int)

# New Technologies

Next-generation sequencing (NGS) and messenger RNA (mRNA) vaccines are two key technologies that have transformed the level of scientific activity and “speed to prototype” in developing new vaccines and anti-virals. This acceleration played out in public view over the last 2 years as the COVID-19 pandemic sparked a worldwide effort to develop working vaccines and treatments safely and at speed.

Vaccine development has historically been a long and complex process, often lasting 10-15 years and involving a combination of public and private investment. Vaccines are developed, tested, and regulated in, if anything, a stricter way than other drugs. Vaccines may be even more cautiously evaluated than non-vaccine drugs because the number of human subjects involved in vaccine clinical trials is usually orders of magnitude greater. Moreover, post-licensure monitoring of vaccines is rigorous globally, whether by the CDC, the FDA, the EMA or another regulator.

As a cautionary example, the very first vaccine for Malaria, despite relatively modest efficacy, was just recommended by the WHO in October 2021, more than 130 years after scientists first identified

the parasite and its complex lifecycle that causes the disease.<sup>9</sup> The rapid progress on COVID vaccines in comparison relied on a series of key advantages. First, the relative simplicity of the infective agent (the targeting of the “spike protein”) and second, the “plug and play” capabilities of the new technologies and the degree of preparedness of global research groups (mRNA, adenovirus-based, etc), especially following the 2014 Ebola and the SARS/MERS epidemics. In addition, the global pandemic crisis meant that the available research dollars were huge, the degree of collaboration as well as the ability to recruit for trials and run them sequentially was unprecedented, and the regulatory approvals process was prioritized.<sup>10</sup>

During global disease outbreaks, scientists have long used genotyping tools to understand pathogens and track genetic changes. This is the process of determining differences in the genetic make-up of an individual by comparing it to a reference sequence. But in recent years, as the sequencing technology has become faster and more affordable, researchers have been able to generate population-level data on pathogen genomes that may be used to help develop more effective vaccines and treatments.

Genome sequencing has also facilitated, for the first time, the ability to investigate the mechanisms that really underpin pathogenesis, that is, the manner of development of a disease. Genomics, transcriptomics, metabolomics, structural genomics, proteomics and immunomics are being exploited to perfect the identification of targets, to design new vaccines and drugs, and to predict their effects in patients. Furthermore, human genomics and related studies are providing insights into aspects of host biology that are important in the study of infectious diseases. This ever-growing body of genomic data and novel genome-based approaches are critical to the timely development of vaccines and of therapeutics to control emerging infectious diseases.

When selecting the antigens<sup>11</sup> to include in a vaccine, scientists typically monitor the most prevalent circulating strains of a disease in order to improve the chances of developing an effective vaccine formulation. Vaccination works by presenting a whole virus, or pieces of it, to the immune system in a way that avoids triggering a full-blown infection. (mRNA vaccines induce cells to produce a protein important in the virus structure to induce the same effect.) This triggers the body to produce antibodies specific to the virus so that the body is primed to act immediately if it were to encounter the real virus in the future. The advent of massively parallel next-generation sequencing (NGS) and the ability to quickly sequence and analyse DNA and RNA has helped advance the understanding of the genetics behind vaccine response and subsequent vaccine development research. Using whole-genome

sequencing data helps ensure the vaccine has the most up-to-date coverage of different strains.

In addition to leveraging NGS technology, the mRNA vaccines could be brought to market quickly in the COVID pandemic as they can be made more easily and faster than traditional vaccines and in smaller, less specialized laboratories. Messenger RNA (mRNA) is the molecule that carries genetic information around our cells, copying it from DNA and acting as a template from which proteins are assembled. It is also what the genome of many viruses – including coronaviruses – is made of. mRNA vaccines are chemically synthesized without the need for cells or pathogens and carry the information that allows our own cells to make the pathogen’s proteins or protein fragments themselves. Importantly, mRNA vaccines only carry the information to make a small part of a pathogen. From this information, it is not possible for our cells to make the whole pathogen.

The idea for this type of vaccine has been around since the 1990s but it did not become possible to make synthetic RNA that did not trigger an unwanted immune reaction until 2008. The first human trial of any mRNA vaccine was in 2013, and the COVID-19 pandemic saw their first authorized use for human use.<sup>12</sup>

9 <https://www.who.int/news/item/06-10-2021-who-recommends-groundbreaking-malaria-vaccine-for-children-at-risk>

10 <https://www.bbc.co.uk/news/health-55041371.amp>

11 That is, the foreign substance which induces an immune response in the body

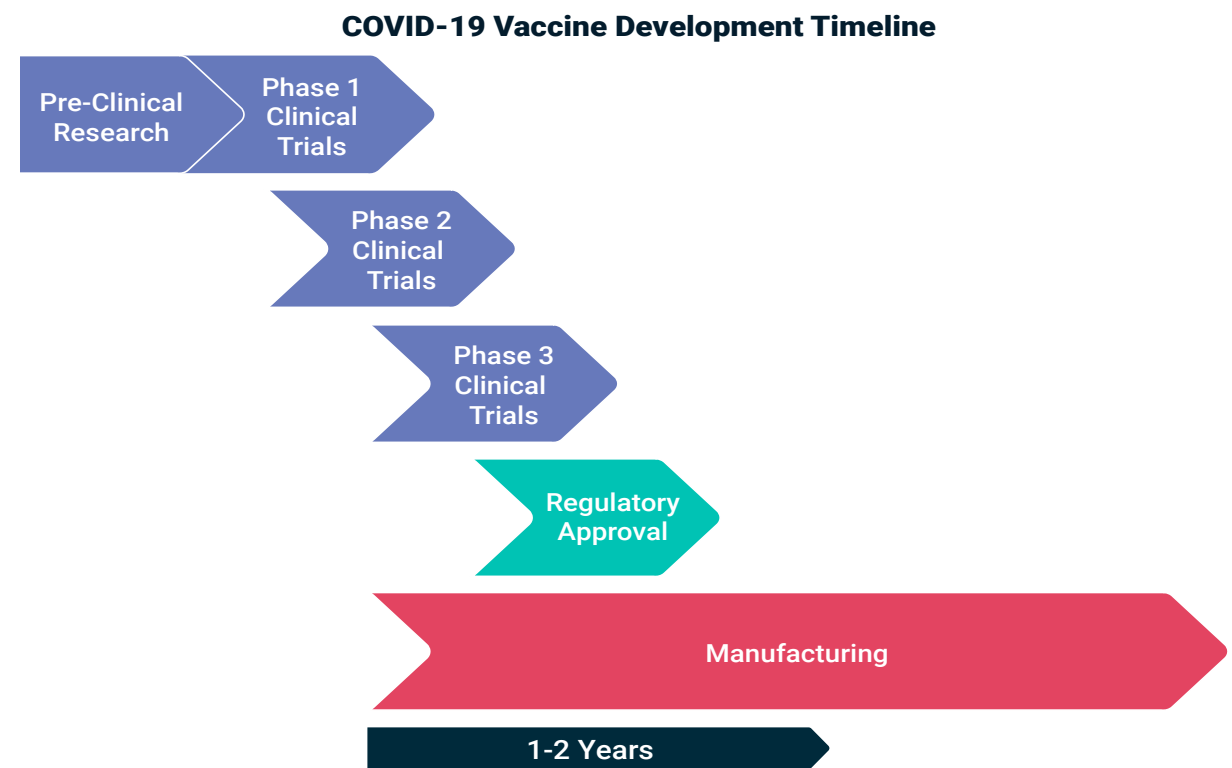
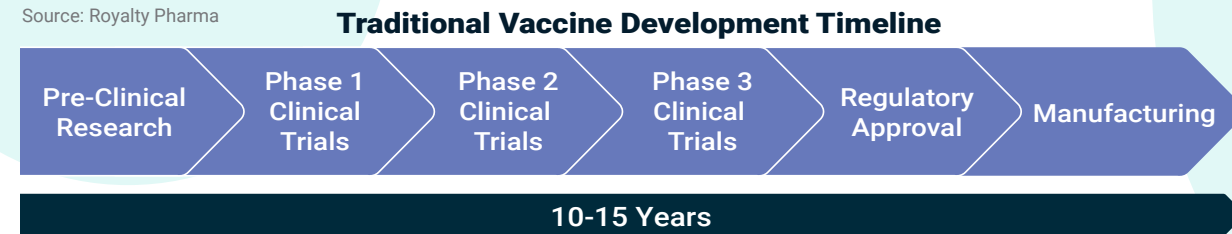
12 <https://publichealth.jhu.edu/2021/the-long-history-of-mrna-vaccines>



The Covid-19 vaccine became available less than a year into the pandemic. Vaccine development usually takes 10 to 15 years, but thanks to a number of factors including the acknowledgement that Covid-19 was a serious concern, a widespread collaboration between scientists and medical experts around the world, government funding, availability of research volunteers, manufacturing vaccine at risk before agency approval, and moving through the approval process in parallel rather than serial steps, this timeline was greatly reduced.

**Exhibit 4:  
How Covid-19 Vaccines Were Able to be Developed So Quickly**

Source: Royalty Pharma



# Unmet need and the research landscape

Despite modern tools and the improved understanding of biology, there still exists a significant unmet need for vaccines and antivirals.

The vaccine successes against Covid have been a remarkable scientific achievement but it remains essential to pursue antiviral drug development alongside vaccines. In most cases, there will likely remain a lag between the outbreak of a new epidemic or pandemic and the delivery of an effective vaccine. During that delay, antiviral drugs can serve as primary tools to keep vulnerable groups safe and for patient care.<sup>13</sup> The impact of the Omicron variant of the COVID-19 virus is a clear illustration of how viruses can evolve to become more transmissible and harder to contain.

Moreover, in cases where effective vaccines have been so far challenging to create – such as HIV, the virus that causes AIDS and HCV, the virus that causes hepatitis C – antiviral drugs are a cornerstone of the therapeutic protocols.

Infectious processes can also play important roles in other diseases such as autoimmune or neurodegenerative disorders. For instance, recent studies have suggested that Epstein-Barr Virus infections can interact with the host immune system to predispose an individual to develop multiple sclerosis. This and other recent advances further enhance the size of the opportunity at play here.

Respiratory failure due to COVID-19 caused widespread mortality, especially in 2020, creating an urgent need for effective treatments and a long-term need for antivirals for future emergent coronavirus pandemics. An effective antiviral that has broad activity against coronaviruses would decrease the impact of future emerging coronaviruses by preventing deaths and slowing viral transmission while public health measures are put into place and vaccines are developed.

<sup>13</sup> <https://hbr.org/2021/02/we-need-to-start-investing-in-antiviral-drugs-for-the-next-pandemic>

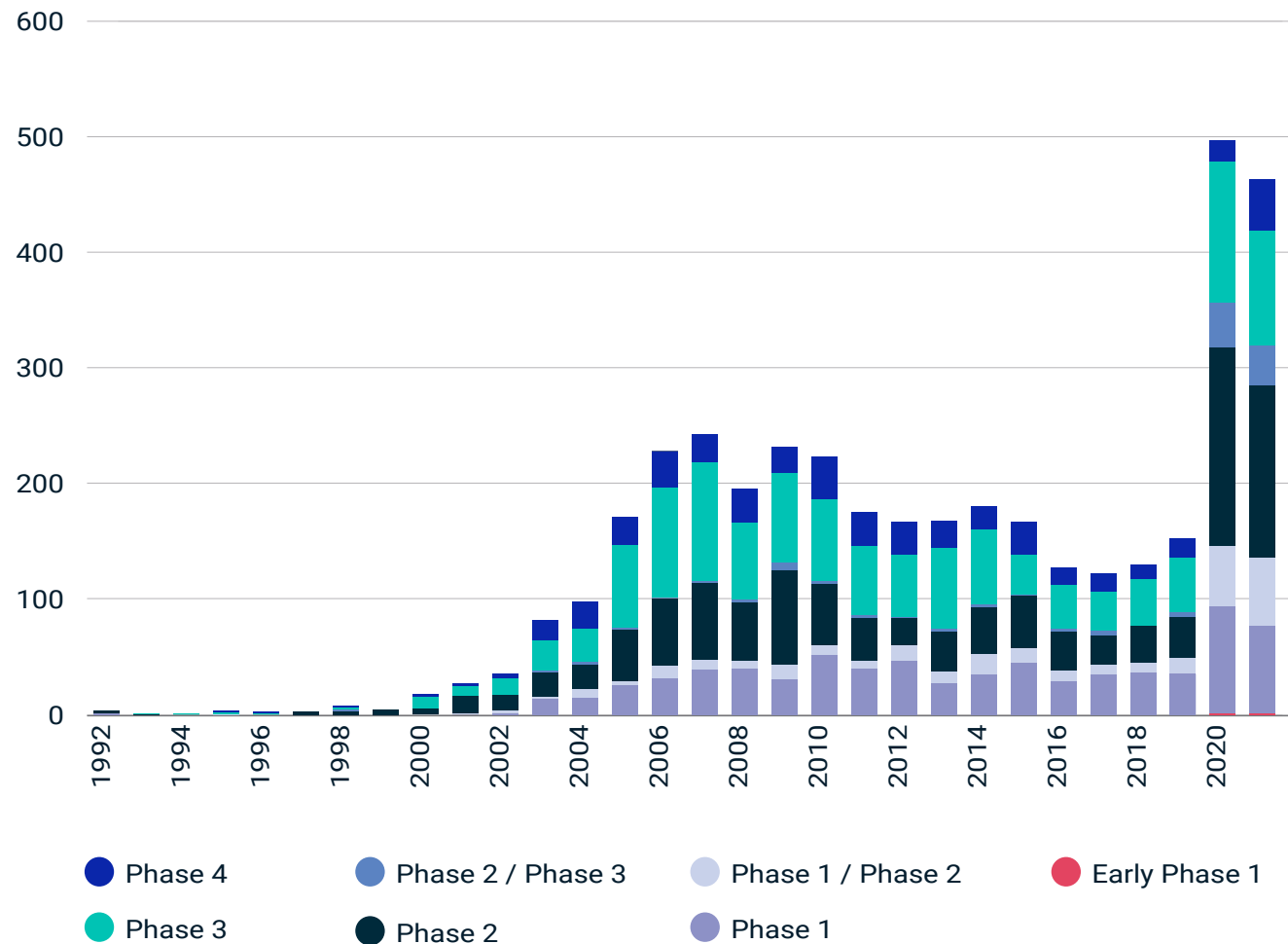
Ironically, the pandemic that brought such focus to vaccine development, has also led to outbreaks of viruses that were almost eradicated because of the disruption of preventive health services including routine childhood immunizations. For example, in 2022, Polio has reemerged in Malawi for the first time in over 30 years<sup>14</sup>, and several cases of monkey pox have been identified in an outbreak in the UK<sup>15</sup> that has already seemingly

spilled across the Atlantic.<sup>16</sup> All told, research in vaccines and antivirals now has a renewed sense of urgency, and one that will need to be central part of public policy for governments worldwide.

14 <https://www.politico.com/newsletters/politico-nightly/2022/03/28/polios-back-blame-covid-00020977>  
 15 UK monkeypox outbreak 'unprecedented' as officials say sexual contact likely route of transmission (yahoo.com)  
 16 Monkeypox: CDC and Massachusetts health officials investigating a case - CNN

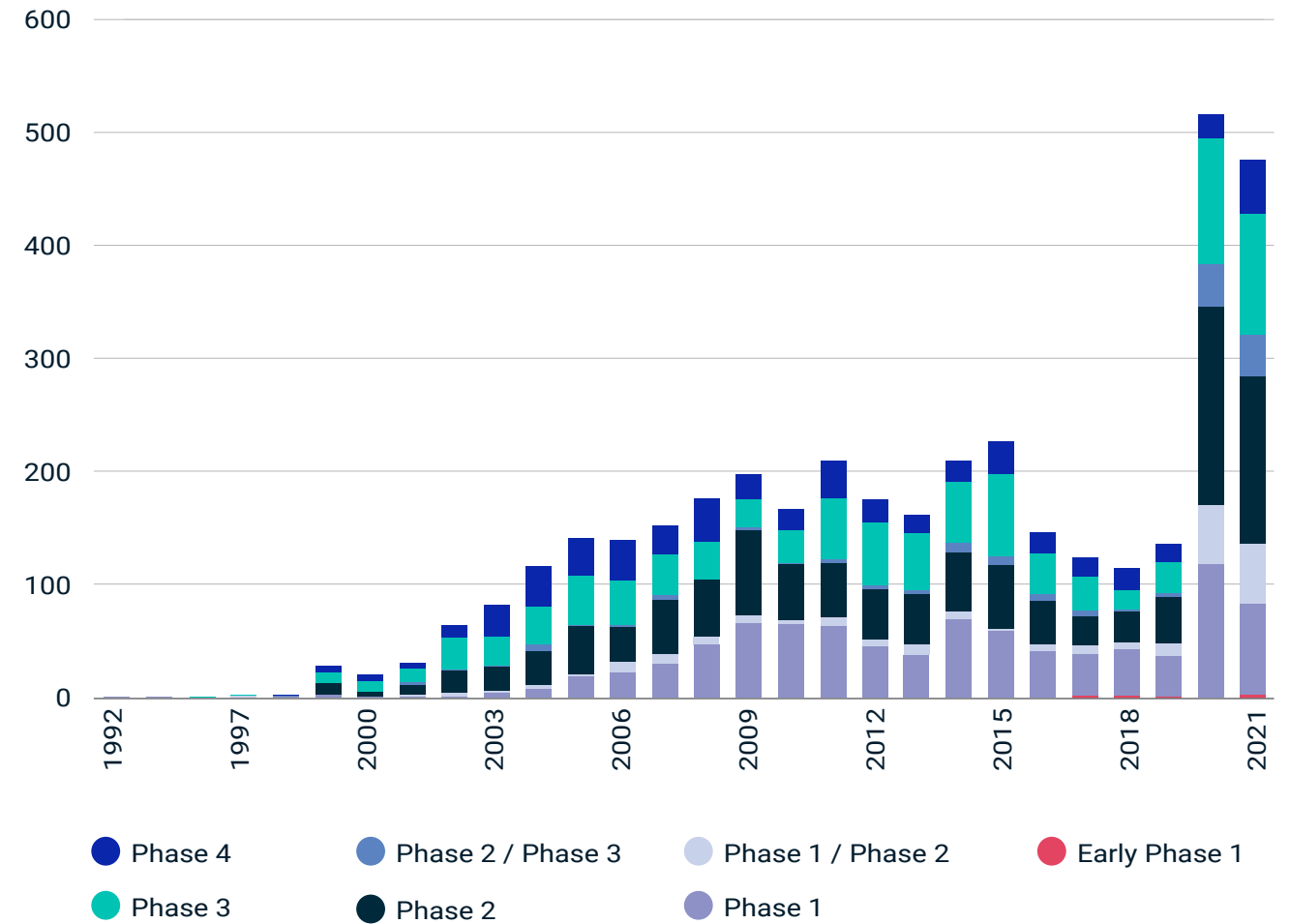
**Exhibit 5:**  
**HIV, Respiratory and Viral Infection Vaccine Clinical Trials by Start Date**

Source: Evaluate Data



**Exhibit 6:**  
**HIV, Respiratory and Viral Infection Anti-Viral Clinical Trials by Start Date**

Source: Evaluate Data



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