

British Society for Immunology

Protecting the world

Celebrating 200 years of UK vaccine research



About the Society

The British Society for Immunology is the leading UK membership organisation working with scientists and clinicians from academia and industry to forward immunology research and application around the world. Our friendly, accessible community consists of more than 4,200 immunologists, giving us a powerful voice to advocate for immunological science and health for the benefit of society.



Celebrate Vaccines is an initiative from the British Society for Immunology to highlight the importance of vaccination in improving global health. Vaccination is one of the most effective public health interventions there is. Through this project, we aim to bring the voice of UK vaccine researchers to the public narrative by examining the past, present and future contributions made by UK-based researchers to global vaccine development. With the 2020 Gavi Replenishment Conference on the horizon, the world now has an opportunity to support their next strategic cycle which aims to immunise 300 million children and save more than 7 million lives.

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What is a vaccine?

Vaccines are protective treatments that prevent disease by training the body's immune system to recognise and respond to infectious pathogens such as bacteria, viruses and parasites to stop you getting sick. This protection can be short-lived or life-long, depending on the type of vaccine and the disease. Some vaccines contain weakened (attenuated) or inactivated versions of infectious agents, particularly viruses. Others contain molecules that mimic specific components of pathogens or toxins produced by bacterial infections.



A rich tradition of life-saving research

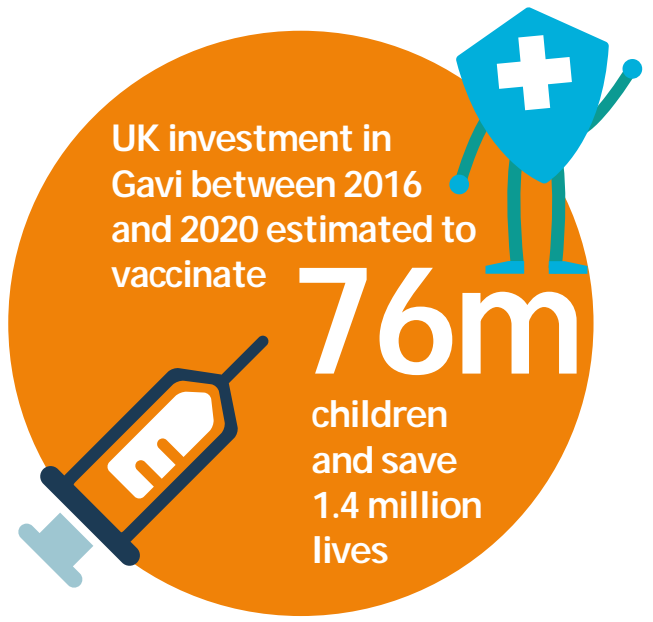
Over the past two centuries, UK scientists have taken the lead in the fight against infectious diseases. Their work spans every aspect from fundamental research into immune responses and pathogen biology all the way through to developing, testing and providing access to vaccines that have saved countless lives. This runs alongside diligent epidemiological work to track outbreaks and identify those at risk.

Today's vibrant UK bioscience ecosystem fosters effective collaboration between industrial, academic, charitable and government-funded research, leveraging global connections to bring novel vaccines to the places that need them most.

Building on a tradition of innovation from the earliest days of smallpox inoculation and the first flu vaccines, our researchers are tackling life-threatening old foes like tuberculosis, new pathogens like the SARS-CoV-2 coronavirus, and laying the foundations to tackle diseases that are as yet unknown to science. New approaches based on fragments of genetic code are coming down the pipeline, offering a faster route to the development and delivery of vaccines against existing and emerging diseases, and enabling the global health community to respond more quickly in outbreak situations.

Vaccination is one the most successful and cost-effective public health measures we have, after clean water and sanitation, preventing an estimated 2-3 million deaths every year. In 1974, only 5% of the world's children were protected from six killer diseases targeted by the World Health Organization. Today, that figure is 86%, with some low and middle-income countries reaching more than 95% immunisation coverage. In total, there are 26 vaccine-preventable diseases, and 20 more in the current global vaccine development pipeline.

Despite this success, there is no room for complacency. Millions of children and adults all over the world are still at risk from preventable diseases because they don't have access to existing vaccines. Hesitancy around childhood vaccination is risking the return of deadly diseases in communities that were previously protected. And there are also plenty of diseases against which there are no effective vaccines, with new threats like Ebola and SARS-CoV-2 emerging all the time. The fight must go on.



Two centuries of pioneering research

For the past two hundred years, researchers in the UK have taken a leading role in developing new vaccines to tackle an ever-growing number of infectious diseases. It's a legacy that started with the first smallpox vaccine in 1796 and continues to the present day.

1800-1890: Widespread infection and vaccine research begins

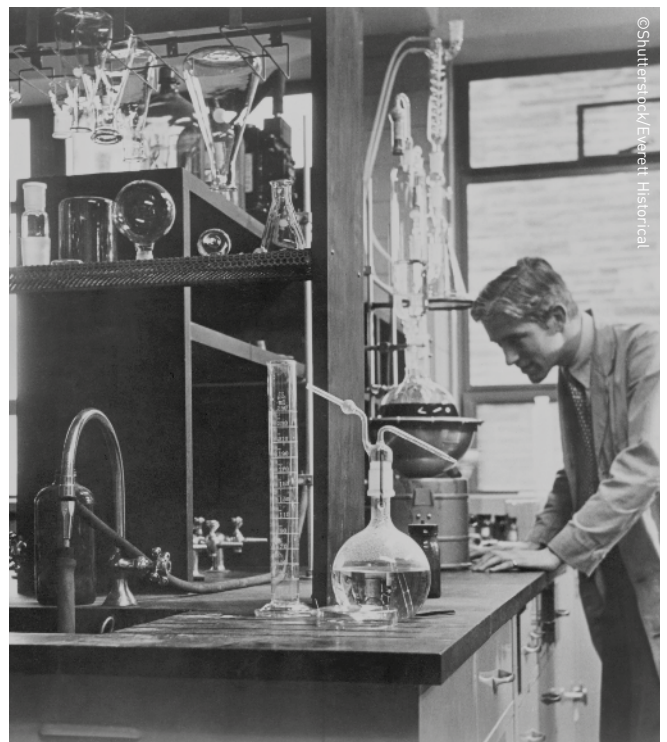
A succession of deadly cholera pandemics began in India in 1817, quickly spreading around the world. In 1854, English doctor John Snow traced a cholera outbreak to a London water pump, confirming that the disease was spread through contaminated drinking water. By 1879, French scientist Louis Pasteur was using attenuated whole cholera bacteria as a vaccine against the disease. The decades that followed saw an intense period of research into the causes of infectious diseases and ways to counter them, with scientists in the UK, USA, France, and Germany all working to create vaccines against diseases like typhoid, plague, tuberculosis, and rabies.

1890-1930: Deactivated toxins used for vaccination

Tetanus and diphtheria are both caused by bacteria that produce toxins. In the early 1900s, Alexander Glenny and Barbara Hopkins at the Wellcome Research Laboratories in London and others began experimenting with vaccines created from deactivated toxins (toxoids), rather than whole bacteria. They developed a toxoid diphtheria vaccine in 1923 followed by a tetanus vaccine in 1926.

1930-1960: The first flu vaccines and the start of global surveillance

Influenza has been responsible for several lethal global pandemics, including the 'Spanish flu' of 1918-20 which caused 21 million deaths worldwide, and it still kills more than half a million people around the world every year. In 1933, English scientists from the Medical Research Council isolated the influenza virus for the first time, eventually producing vaccines that were first trialled with British army troops fighting in World War II.



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There are many different subtypes of influenza virus, all of which are continually mutating and evolving. Although modern flu vaccines contain multiple viral subtypes, providing better protection, they may still be ineffective against the next season's disease. A global influenza surveillance program was established by scientists from the Medical Research Council in 1947 to monitor the changing viruses and develop more effective seasonal flu vaccines.

1950–2000: Cell techniques spark a new era of vaccine research

In the 1950s, American scientist Jonas Salk developed new techniques to grow polio viruses in cells in the laboratory without the need for animal hosts. He used this method to produce a polio vaccine made from deactivated viruses, halting the polio epidemic in the USA and saving thousands of lives.

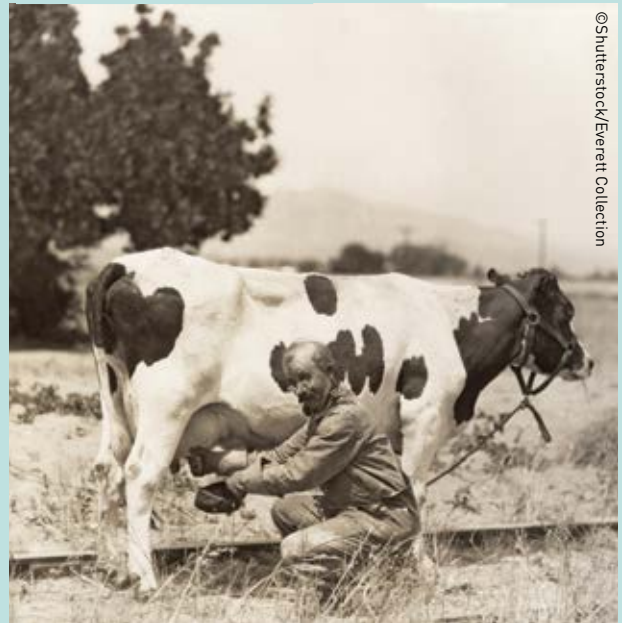
Following the success of Salk’s polio vaccine, many researchers in the UK and around the world also adopted cell culture techniques. As a result, this era saw new vaccines for a range of viral diseases, including measles, mumps, rubella, and Japanese encephalitis.

1970–2020: Genetically engineered proteins bring further advances

Glenny and Hopkins’ work on toxoid vaccines in the 1920s showed that whole bacteria weren’t necessary for creating immunity. But it wasn’t until the 1970s that researchers worked out how to turn specific molecules from the outer coats of bacteria and viruses into vaccines. By the 1980s, researchers began using genetic engineering to produce precisely tailored molecules as vaccine components, known as conjugate vaccines. The first of these vaccines, designed against hepatitis B, was approved in 1986. A more recent success came in 2019 with the roll-out of the first typhoid vaccine suitable for infants.

Thanks to the dedicated work of researchers all over the world, vaccines now prevent 2–3 million premature deaths every year.

Case Study



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From vaccination to eradication: the story of smallpox

Nobody under the age of 40 has ever seen a case of smallpox, and the first steps towards that victory happened right here in the UK.

In 1774, a village in Dorset called Yetminster was struck by a smallpox epidemic. It was known that farm workers who had experienced less serious cowpox were immune to smallpox, so an enterprising farmer, Benjamin Jesty, scratched his wife and children’s skin with pus from his cow’s cowpox blister in the hope of protecting them. While his family stayed safe, Jesty didn’t verify or publish his results.

Twenty years on, Gloucestershire doctor Edward Jenner inoculated eight-year-old James Phipps with material from a cowpox sore on a milkmaid’s hand. Two months later, Jenner treated Phipps with pus from a smallpox blister. Reassuringly, the boy remained unaffected by smallpox, proving the protective effects of cowpox against the disease.

Jenner tested more children, including his own infant son, and published his findings in 1798. His new ‘vaccination’ – named after vacca, the Latin word for cow – was widely adopted and refined over the following years.

Jesty and Jenner’s work paved the way for the global smallpox vaccination program. After causing countless millions of deaths over thousands of years, the disease was finally declared eradicated in 1980.

There are now

26

vaccine-preventable
diseases

Over 200 Years of Vaccination 1750 – 2025



1774

Benjamin Jesty, a farmer from Devon, inoculates his family against smallpox using cowpox material (UK)

In 18th century Europe
400,000
people died from smallpox every year

1853

Introduction of compulsory smallpox vaccination for babies in England (UK)

1879

Louis Pasteur develops the first bacterial vaccine against cholera (France)

1750

1775

1800

1825

1850

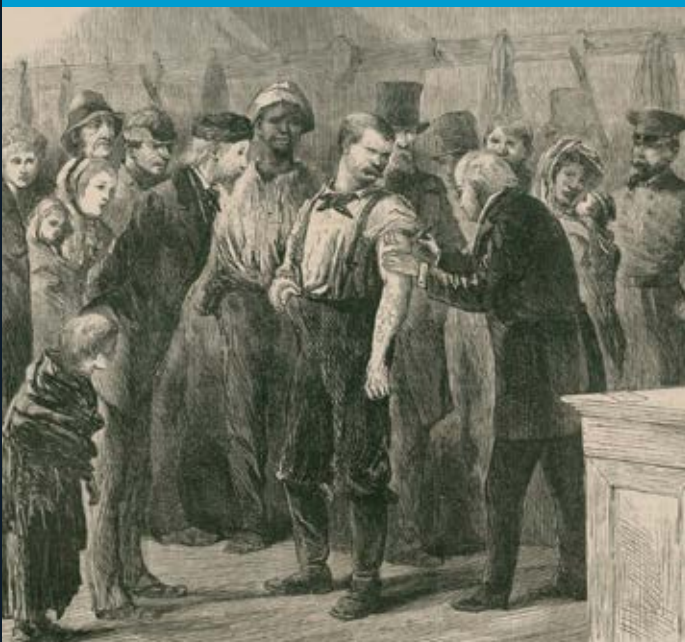
1875

1796

British doctor Edward Jenner uses material taken from cowpox lesions to create the first smallpox vaccine and two years later publishes his first work describing smallpox vaccines (UK)

1836

English doctor Edward Ballard introduces a more potent smallpox vaccination (UK)



1896

Almroth Wright introduces a typhoid vaccine for troops (UK)



1891

English physician S. Monkton Copeman uses glycerine as a germicide in vaccines to increase safety (UK)



1933

Scientists at the Medical Research Council develop a new flu vaccine, first used to protect soldiers in World War II (UK)

1900

1923

Alexander Glenny and Barbara Hopkins develop new type of diphtheria vaccine (UK)

1947

Global influenza surveillance program established (UK)



0
1980: World Health Organization declares smallpox eradicated

1986

First vaccine produced by genetic engineering techniques approved for hepatitis B (Chile/USA)

1958

Sam Katz tests the first measles vaccine (USA)

1950

1988

MMR vaccination rolled out across the UK

1975

2002

Polio eliminated from Europe



2019

First Ebola vaccine prequalified by World Health Organization for rapid rollout in affected countries

2006

First vaccine approved for human papillomavirus, which causes a range of cancers

2000

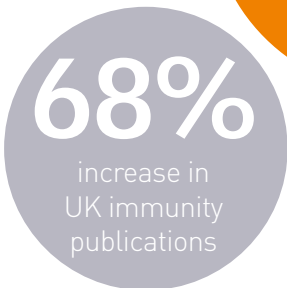
2015

Programme to vaccinate all newborn babies against meningitis B starts in the UK

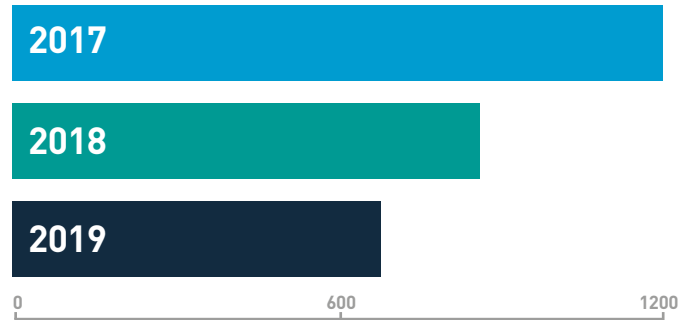
2025

UK research is leading the world

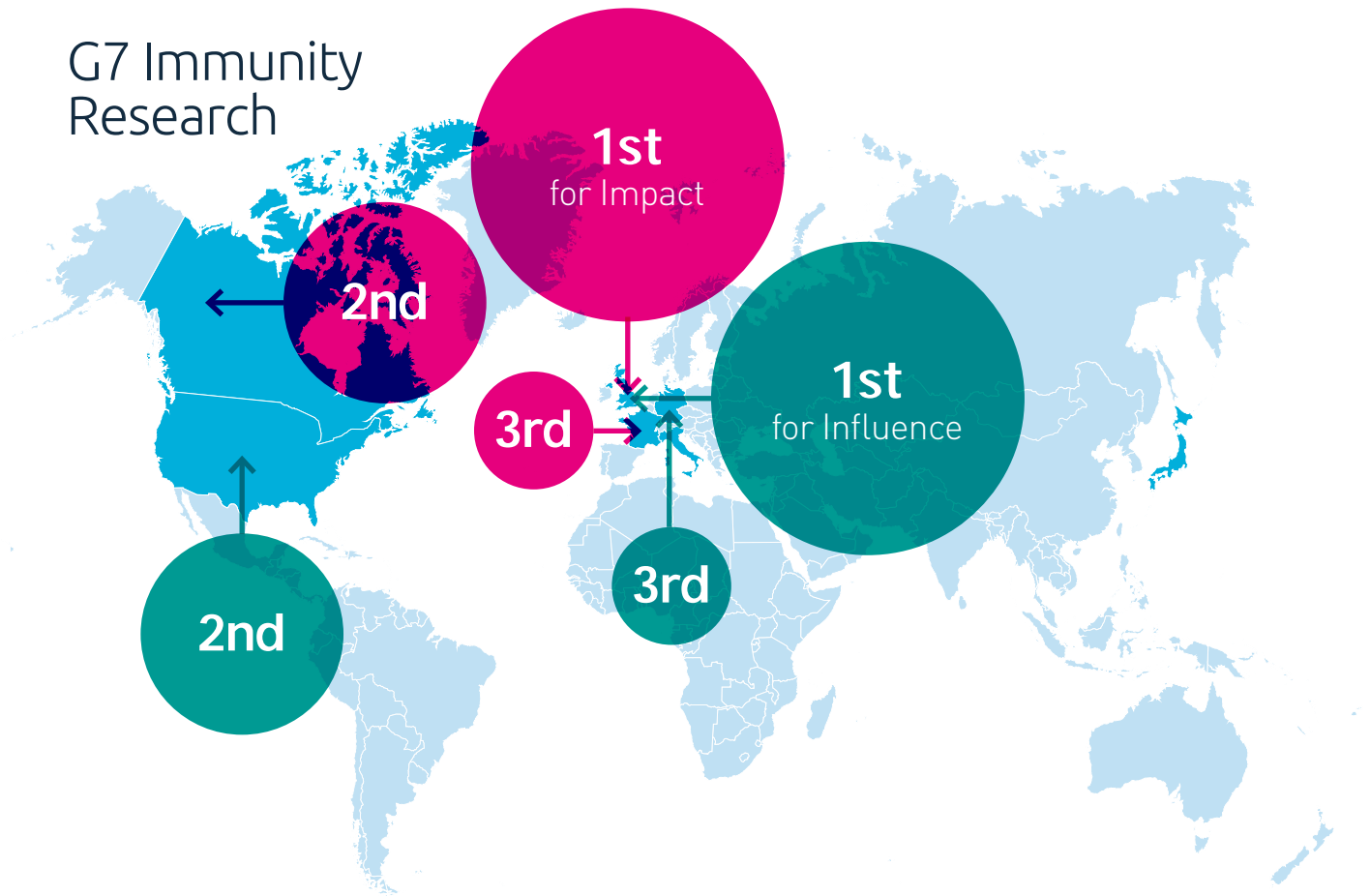
The UK has been at the cutting edge of science for centuries, and research into immunity and vaccination is no exception. From understanding the immune system to tracking infections, developing new vaccines to life-saving clinical trials, our researchers are making a major contribution to global progress in public health.



Number of grants awarded by top 10 funders of UK vaccine R&D



G7 Immunity Research



Despite its relatively small size, the UK punches well above its weight when it comes to producing world leading research, particularly around the science underpinning immunity.

When comparing UK immunity research performance to other G7 countries, the UK consistently outperforms its peers in terms of the volume and influence of research outputs relevant to vaccines.

The UK contains around 9% of the G7 population, and yet produces 14% of the G7's scientific publications in immunity. The UK also leads the G7 in terms of the impact of these publications, indicated by the number of times the results are cited in other research papers. UK publications on immunity are cited on average 29.3 times. The UK's Fields Citation Ratio, a measure of the scientific influence of those publications, is also the highest of all G7 countries.

In 2017 the UK published 8,630 scientific papers in immunity, an increase of almost 68% from the 5,141 published in 2008, making the UK the fastest growing country of the G7 in this area. However, research specifically focusing on vaccines is lagging behind immunity research in the UK in terms of performance and influence. At a time when the world is acutely aware of the threats posed by emerging diseases, it is concerning to see that the number of grants awarded for vaccine research and development in the UK appears to have taken a downturn over recent years. When vaccine research is more important than ever before, we must ensure that efforts are being undertaken to bring vaccine research to parity with the rest of the immunity sector. The effect of the recent downturn in grants being made to vaccine research is yet to become clear.

The importance of UK immunity research to local and international policy is highlighted by the fact that the World Health Organization (WHO) and the UK Government are heavily reliant on homegrown science, with the WHO citing UK research as their number two source of immunity information and the UK Government using it as its number one source.

A report by the All Party Parliamentary Group on Global Health, published in February 2020, also highlighted the quality and impact of UK research, placing the UK at the top of the G7 across multiple health research disciplines, including immunology.

Immunology research was shown to outperform other health research disciplines in the UK, with a higher citation score than the UK's public health and healthcare sciences sectors. UK immunology also ranked higher amongst the G7 compared to our research and experimental medicine sector.

The same report estimated that the UK's investment in Gavi, the Vaccine Alliance, between 2016 and 2020 enabled 76 million children to be vaccinated and saved 1.4 million lives. According to the WHO, Gavi has averted medical costs of \$350 billion and brought \$820 billion in economic and social benefits since 2000 across the 73 countries it has operated in. The importance of vaccine research to patient benefit, not just in the UK, but across the whole world is clear. It is evident that maintaining the UK's status as the engine room of immunity research and levelling up its vaccine research sector is key to increasing the number of diseases which we can protect ourselves against using vaccines.

An ecosystem for innovation

The UK has long been a world leader in vaccine research, from the earliest days of smallpox vaccination to tackling recent outbreaks such as Ebola and COVID-19. This strength comes from a broad biomedical research ecosystem combining a rich tradition of academic research into epidemiology and immunology with a thriving industrial sector, supported by national and international philanthropic and government funding.

The UK is home to several major academic institutions focused on researching and preventing infectious diseases, including the Jenner Institute at the University of Oxford, the Vaccine Network at Imperial College London, the London School of Hygiene and Tropical Medicine, the Liverpool School of Tropical Medicine, and Public Health England's research facility at Porton Down. In addition, there are numerous institutes, departments and research groups within universities across the nation whose work touches on all aspects of vaccine research.

The academic research community collaborates closely with companies in the pharmaceutical and biotechnology industry, both at home and abroad. These combined efforts translate bright ideas into commercial-grade products that are suitable for clinical trials, large-scale manufacture and regulatory approval.

This flourishing research ecosystem is supported by funding from a range of sources including the UK Government, which funds the overarching UK Vaccine Network and subsidiary specialised research networks. Support also comes from the European Union and non-profit and charitable organisations such as the Wellcome Trust and the Bill & Melinda Gates Foundation.

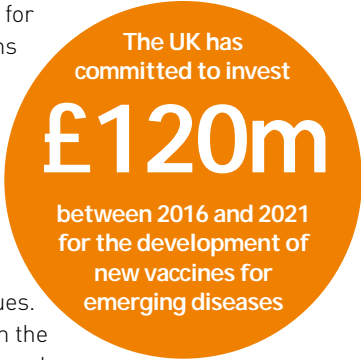
Past progress, future hopes

One of the UK's greatest scientific strengths is in the field of immunology research. This ranges from fundamental research into the pathogens that cause disease through to understanding how the immune system builds immunity against them. Detailed structural biology studies are also helping us to discover the precise conformation of vaccine components to find those that will trigger the most protective immune response.

We also have particular expertise in maternal, fetal and newborn immunology, studying the immunological 'conversation' between mother and child. One important area is the role of vaccination in the later stages of pregnancy, which protects young babies once they're born. This approach has led to a significant reduction in deaths from whooping cough (pertussis) in the UK, providing a shining example for the rest of the world to follow.

Epidemiology is another area where the UK has excelled for more than 150 years, enhanced by modern DNA sequencing technology. This vital data reveals how new outbreaks arise and spread, informs decision-making about which diseases or at-risk groups should be targeted by vaccines, and shapes strategies for vaccination in outbreak situations or where better utilisation of existing vaccines could make a big difference to public health.

UK scientists are also hard at work developing the next generation of tools and techniques. These include vaccines based on the genetic code of pathogens and novel immunisation methods like harmless genetically engineered viruses. This is fuelled in part by the rise of gene editing tools such as CRISPR, creating more precise manipulations of bacterial and viral components and triggering the immune system to generate a potent protective effect. There is also significant interest in new approaches for combining, storing, transporting and delivering vaccines to make sure they are as efficacious and accessible as possible.



Case Study

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In the UK we benefit from a rounded, complete approach to vaccine development, along with clear vision and leadership”

Professor Andrew Pollard, University of Oxford

From the UK to the world

In the UK, we benefit from a rigorous schedule of childhood immunisation, along with vaccines for other groups. This includes seasonal flu vaccines for children, the elderly or vulnerable, and teenage vaccination against human papilloma virus (HPV), which can cause a range of cancers. Our position at the forefront of vaccine research often means that the UK population directly benefits from early access to novel vaccines. For example, we were the first nation in the world to roll out new vaccines against Meningococcal B and C following large-scale UK trials.

But reducing death and disability from vaccine-preventable diseases is a global health challenge, and one that is ever more pressing in a fast-changing and interconnected world. The UK provides significant funding for research into vaccinating against diseases in low and middle income countries, including the £1.5 billion Global Challenges Research Fund, administered by UK Research & Innovation (UKRI). Not only does this save lives and reduce inequality in the poorest parts of the world, but also acts at a distance to protect the health, safety and economy of our own country from the risk of new outbreaks in the globalised world in which we now live.

During the 2013-16 Ebola outbreak, UK researchers played a vital role in monitoring the spread of the disease, studying the virus in detail and developing new vaccines which were first tested in the UK before deployment in West Africa. Similarly, during the 2009-10 H1N1 swine flu pandemic, some of the first vaccine trials were undertaken in the UK. The results helped to shape global health policy through the World Health Organization, as well as our national response.



Tackling antimicrobial resistance through vaccination

Professor Adam Cunningham from the University of Birmingham is co-chair of the BactiVac Network, set up to address the challenges of developing vaccines against bacterial infections.

Bacterial infections kill around six million people each year, with a disproportionately high number of fatalities occurring in low- and middle-income countries. Concerningly, many dangerous bacteria are now developing resistance to antibiotics – so-called ‘superbugs’ – making them even more deadly.

“Vaccinations can remove the need for antibiotics by priming the immune system to eliminate the pathogen before an infection takes hold,” explains Cunningham. “Bacteria can quickly develop resistance to antimicrobial drugs, particularly when they are overused, but resistance to vaccines is largely absent.”

We already have several vaccines against bacterial diseases, including tetanus, pertussis and typhoid. Cunningham hopes that BactiVac can accelerate the development of vaccinations against some of the deadliest remaining bacterial diseases, including those caused by *E. coli*, *Salmonella*, *Shigella* and pneumococcus.

“There’s great expertise across the UK and internationally in bacterial vaccinology, but there are also lots of big questions and unknowns in the development process,” he says. “We’re bringing together individuals to share expertise, fill in knowledge gaps, break down barriers and push new vaccines along the development pipeline, so we don’t have to keep relying on antibiotics.”

Working together for global health

Throughout the 20th century, UK researchers have built a strong network of international collaborators and partnerships, although it has tended to be focused on a relatively small number of countries. As our world becomes increasingly connected, bringing new opportunities for international scientific exchanges and training, it's easier than ever before to forge partnerships and collaborations wherever they are needed.

In the past, many vaccine research projects in lower-income countries where many of the studied diseases are endemic were carried out by visiting teams of European or American scientists. Today, most of the pioneering research projects and papers published on vaccine research have a long list of scientists and institutional partners drawn from many countries, including across Africa and Asia. Working together with scientific organisations in these regions enables UK researchers to share expertise and resources, and creates new opportunities to empower and upskill local scientists.

UK research brings vaccines where they're needed

New vaccines are often developed in higher income countries like the UK and do eventually reach low- and middle-income countries (LMICs), but logistical and financial challenges mean that this process can take a long time. For example, the first conjugate pneumococcal vaccines were licensed in Europe twenty years ago, but they still are not available everywhere.

UK research and funding are vital for speeding up the availability of vaccines in LMICs. International organisations like Gavi, the Vaccine Alliance, have been instrumental in making vaccines commonplace in these countries, with strategic funding from the Wellcome Trust and MRC also

playing a significant role. These efforts have increased vaccine coverage globally, with 86% of infants worldwide now receiving the diphtheria-tetanus-pertussis vaccine.

Harnessing the 'network effect'

Current vaccine development pathways are expensive, complicated and convoluted, with each new product often taking 10–15 years to come to fruition. Delays and challenges during the development process can stop life-saving vaccines from ever making it to market. Networks that bring together international experts from industry, academia, philanthropy and government can help overcome these roadblocks and deliver crucial vaccines where they are needed most.

The UK leads five vaccine research networks:

- The **VALIDATE** Network is working on vaccinations for diseases caused by complex pathogens like tuberculosis, leishmaniasis, melioidosis, and leprosy
- The **IVVN** Network is focusing on developing veterinary vaccines for diseases affecting agriculture in low- and middle-income countries
- The **HIC-Vac** Network supports human infection challenge studies to accelerate vaccine development
- The **IMPRINT** Network is developing safe and effective vaccines for pregnant women and newborns
- The **BactiVac** Network is accelerating the development of vaccines for bacterial diseases



We have been amazed by the sheer enthusiasm for the Network among our international colleagues. It has grown extraordinarily rapidly, and we now have members in around fifty countries all over the world



Dr Beth Holder, IMPRINT Network

“

My heart beats for science in Africa”

Professor Faith Osier, Group Leader, KEMRI-Wellcome Trust Research Programme

Despite the challenges associated with coordinating such large international networks, they have been very successful and sprouted collaborations that have impacted research around the globe. Besides bringing together experts to share ideas and resources, the networks also provide small research grants for overcoming research hurdles or generating pilot data. They also play a vital role in building research capacity in LMICs by providing post-doctoral fellowships, collaboration opportunities and training for early-career researchers.

From Nepal to the world

Professor Andrew Pollard from the University of Oxford has been tracking infectious diseases in Nepal for 15 years. After identifying typhoid as one of the commonest killers of under-fives in the country, he and his collaborators developed a new conjugate typhoid vaccine that was first tested in the UK and manufactured by the Indian company Bharat Biotech International.

The vaccine underwent large-scale trials in Nepal and elsewhere in Asia and Africa, with interim results showing that it reduced typhoid infections by an impressive 82%. In 2019, the vaccine was employed by the Pakistani health authorities to tackle an outbreak of antibiotic-resistant typhoid. Following its success, the vaccine is now being rolled out to many more countries including Zimbabwe and Liberia, supported by Gavi, the Vaccine Alliance.

Case Study



An army of African scientists

Professor Faith Osier is a group leader at the KEMRI-Wellcome Trust Research Programme in Kilifi, Kenya, where she's working on promising malaria vaccine candidates. She established the SMART consortium, bringing together scientists from seven African countries to share resources, training and data to support malaria vaccine research.

Osier also works closely with UK institutions, including the Wellcome Sanger Institute, the University of Cambridge, the University of Oxford and the London School of Hygiene and Tropical Medicine. "Our collaborators in the UK provide access to high-end technology that we do not have or that we cannot get working quickly here, including technologies like sequencing, proteomics, and structural biology," she says. "They also support the training of African scientists, allowing students to visit and work in their laboratories and learn new technical skills."

"My heart beats for science in Africa," Osier admits "We need African scientists to work to eradicate diseases in Africa. I have a vision that African researchers can be involved in vaccine development from the beginning of discovery, to upscaling, conducting trials, regulation, and right through to the end of the process. To do that, we rely on our well-resourced colleagues to support their education and training."

Vital partners in the journey from lab to clinic

The life sciences industry is a key part of the UK economy, worth over £70 billion per year, and plays a crucial role in developing and delivering vaccines both here and abroad. The UK bioscience ecosystem combines a strong academic tradition with robust commercial research - together with stable sources of charitable, government and industrial funding - which all play a part in vaccine innovation.

It takes a global village to create a vaccine

It takes years and costs hundreds of millions of pounds to undertake the journey from a bright idea in the lab to a safe and effective mass-produced vaccine. Industrial partners may have the power, money and scale to develop, test and manufacture vaccines, but they cannot do it alone.

Global networks of manufacturers and funders are vital for the success of vaccines. For example, a recent tuberculosis vaccine was co-funded by GSK, the European Commission, the UK's Department for International Development, and the Bill & Melinda Gates Foundation. The rights to develop the final product now belong to the Bill & Melinda Gates Foundation, so they can make sure it is available in LMICs where the disease is most prevalent.

Although international pharmaceutical companies may have a global focus, they interact closely with researchers in the UK - several global pharmaceutical companies have vaccine research hubs located in the UK, including Pfizer and GSK. Industry relies on academic collaborators for the fundamental research into infectious diseases and immunity that underpins vaccine development. It is also dependent on public health organisations to support the clinical trials that enable new vaccines to reach the people who need them. But this isn't just a one-way flow of information. For example, Pfizer is working closely with the IMPRINT Network, which focuses on maternal and neonatal immunisation, offering lab placements for academic researchers to develop their skills.



When it comes to vaccines, UK pharmaceutical company GlaxoSmithKline is top of the list of industrial collaborators with UK universities

Embracing maternal vaccines

Traditionally, companies have been wary of developing vaccines for pregnant women. But the outstanding success of the maternal whooping cough, flu and tetanus vaccines proves that research into immunisation during pregnancy can have a major impact on public health. Maternal vaccines now feature heavily in the development pipelines of many companies, targeting diseases such as group B streptococcus and respiratory syncytial virus (RSV).

RSV is a major cause of childhood deaths, particularly in poorer countries, and kills around 60,000 children under the age of five every year worldwide. There are currently no approved vaccines for RSV, despite more than 50 years of research, and the World Health Organization has prioritised the development of maternal vaccinations that can protect newborns against the disease. Several companies are now focusing their scientific firepower on RSV and there are numerous candidates currently in development.

“

Everything we do, we do in collaboration. It's a two-way conversation, and we need to have people inside and outside the company on the same wavelength”

Dr Stephen Lockhart, Pfizer

Boosting UK vaccine manufacturing capacity

Another example of collaboration between academic, government and industrial research is the new Vaccine Manufacturing Innovation Centre in Oxfordshire. This is the first facility fully dedicated to the development and manufacturing of vaccines in the UK. It is supported by several leading pharmaceutical companies such as Merck Sharp and Dohme, Johnson & Johnson and GE Healthcare, and academic institutions including the University of Oxford, and UKRI. Announced in 2018 and originally due to be finished in 2022, completion has been brought forward to 2021 to increase UK vaccine manufacturing capacity in response to the COVID-19 pandemic.

Providing accessible vaccines for low- and middle-income countries

Although global vaccine companies make the majority of their profits in high-income countries, they also work to ensure that vaccines are available in the countries where they are needed most.

To support this effort, companies have been researching ways of making prices as cheap as possible and adapting vaccines for smooth delivery in LMICs. Developing products that are easy to ship and store, do not require refrigeration, and are ready-to-use are vital areas of research for many vaccine manufacturers. Several companies, including Pfizer and GSK, have developed multi-dose vials that reduce waste and are easier to transport, reducing the cost of each dose.

Case Study



Meningitis C vaccine: a Great British success story

During the 1990s, there was a series of outbreaks of meningitis around the world caused by group C *Neisseria meningitidis* bacteria. Cases in the UK grew throughout the decade, reaching around 1,500 cases and 150 deaths per year.

Although the first vaccines against the disease were developed in the 1970s, they did not offer lasting immunity and were ineffective in babies and toddlers, so they weren't widely used. Based on the success of a conjugate vaccine for *Haemophilus influenzae* type B (Hib) in the early 1990s, the UK Department of Health redirected vaccine research towards developing a conjugate meningitis C (MenC) vaccine that would be effective for infants and young children.

Three vaccine manufacturers agreed to be involved in the project and co-sponsored clinical trials alongside government-funded researchers, resulting in the world's first MenC vaccine which was licensed in 1999. The Department of Health soon added the vaccine to the childhood immunisation schedule and initiated a catch-up program for older children, reducing cases of meningitis C by 87% by 2001. Other countries soon followed the UK's lead, saving thousands of lives. The MenC vaccine represents a great vaccine success story and shows what we can achieve with proactive collaboration between all parts of the vaccine research community.

Facing the future

Humans have been at war with microbes for millions of years, and they aren't giving up the fight any time soon. Pathogens are constantly changing, evolving with altered characteristics, which presents new challenges to science, healthcare and society. From tracing new outbreaks to developing novel vaccines in a timely way, we must always be on our guard for the next threat.

Within a matter of months of its first appearance in China in late 2019, a novel coronavirus had spread around the globe, upending conventional life and causing the illness, COVID-19, in millions of people. As world leaders grapple to find the best way to respond to this threat, it reminds us that we cannot predict when, where, or what the next infectious epidemic will be. We need to be as ready as we possibly can be to respond to emerging diseases and roll out vaccines to protect against them.

Be prepared

The 2013-16 Ebola outbreak in West Africa caused more than 11,000 deaths and cost at least \$50 billion. Rapid vaccination at the right time and place would have made a huge difference: although a vaccine against the disease had been in development for more than ten years, it wasn't ready to roll out until the epidemic had spread for a year, costing many thousands of lives.

Diseases do not respect borders, so protecting the world's population requires an international effort. The Coalition for Epidemic Preparedness Innovations (CEPI) is a global alliance that funds and coordinates the development of vaccines against emerging infectious diseases, and enables access to vaccines during outbreaks. Prior to the COVID-19 outbreak, CEPI had secured more than \$750 million in investment from many governments and charities, including the UK Government and the Wellcome Trust. In March 2020 the UK Government pledged another £210 million towards the development of vaccines against COVID-19, making the UK the largest individual donor to the coalition.

CEPI is pushing new vaccines through initial safety testing and early-stage clinical trials in order to build a stockpile that is 'good to go' before an epidemic even begins. CEPI is also funding innovative platforms that can accelerate the development and manufacture of novel vaccines in a matter of months rather than years, and working with governments and regulatory agencies to make sure that they can get to the people who need them most.



Novel coronavirus, SARS-CoV-2, emerging from the surface of cells cultured in the lab

Are we ready for 'Disease X'?

The World Health Organization uses the term 'Disease X' to refer to an as yet unknown pathogen with the capacity to cause serious harm to human health. It is understandably hard to predict where any new disease will come from, but we can still do much to build the skills and capacity to respond rapidly when it does.

Consistent investment in immunology and vaccines is the best way to prepare for the next epidemic, but once an outbreak is out of the headlines, the funding for research often dries up. Although it has spread with a lethal ferocity, SARS-CoV-2, the coronavirus responsible for COVID-19, isn't a complete surprise to science. During the SARS outbreak in 2002-04, caused by a coronavirus similar to SARS-CoV-2, several vaccine candidates were identified but the research petered out when the epidemic died down. If research had continued, we might have been better prepared to tackle the related COVID-19 pandemic.

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Over the last five years we've been on a path to expand our capacity for protecting against many of the pathogens that we recognize as threats to global health. One of the things we really need to do going forward is to work out the pathway from the brilliant vaccine discovery work that has happened in the UK all the way through to having products that are licensed and ready to go when they're needed

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Professor Andrew Pollard, University of Oxford

Researchers in the UK and around the world are now racing to develop new vaccines for COVID-19. But it won't be enough to make and test novel vaccines in experimental settings. Indeed, several vaccine candidates are building on the work that was done after previous outbreaks of related coronaviruses, SARS and MERS. Promising products need to be fast-tracked through clinical trials and regulatory approval without compromising on safety or efficacy - even in the midst of a pandemic - and produced on a large enough scale to immunise entire populations.

There has traditionally been little commercial incentive to develop vaccines for diseases affecting populations in small geographic areas in developing countries, or those that only occur in intermittent outbreaks. But in our modern, interconnected world, disease outbreaks in other countries can end up affecting us all, so we need to make sure we're ready to face whatever the future brings.

Case Study



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Making the jump

Most of the recent infectious diseases that have evolved into pandemics originally came from animals. For example, HIV first originated in chimpanzees, while Ebola is thought to have been transmitted to humans from bats. Although the exact animal source of the latest SARS-CoV-2 coronavirus is currently unknown, it is also thought to have originated in bats. Recent global shifts including climate change, habitat destruction, increasing human populations and illegal wildlife and bushmeat trades all make it more likely that pathogens will have the opportunity to make the jump from animals into humans.

There's a vital role here for surveillance and monitoring of human and animal populations in 'hot spot' countries in Africa, Asia and South America in order to spot emerging threats. For example, the Zika virus was first identified in African monkeys in 1947, sixty years before the first widespread outbreak in humans. It's therefore equally important that these concerns are reported to and acted upon by national and international health authorities in a timely way. Failure to do so risks the emergence of other diseases with the potential to escalate to pandemic status, resulting in widespread loss of life, economic damage and geopolitical destabilisation.

Developing the next generation of vaccines

Protecting the health of the global population will need a new generation of vaccines that are effective, affordable and accessible to everyone who needs them - even in the midst of a disease outbreak. Vaccine research has come a long way since Edward Jenner and his cows, but there are still many challenges to be overcome.

Understanding immunity

Vaccines are all based on antigens: molecules derived from pathogens such as bacteria and viruses. They create protection by 'training' the immune system to recognise and respond to the corresponding disease-causing versions.

Identifying antigens with the potential to make an effective vaccine therefore requires deep knowledge of infections and immunity. But we do not fully understand how the immune system responds to different diseases - particularly to complex pathogens like malaria - or how it varies in genetically diverse populations around the world. Even when scientists find a vaccine candidate that elicits an immune response in laboratory tests, there is no guarantee that the vaccine will be safe and effective in human populations.

Human infection challenge (HIC) studies - in which a small number of healthy volunteers are vaccinated and deliberately infected with pathogens under tightly controlled conditions - have a vital role to play in revealing how the immune system responds to disease and the effectiveness of novel vaccines.

Changing the incentives

Every promising new vaccine has to be tested in large clinical trials costing millions of pounds. Even at this stage there is a chance that the vaccine will not be effective or will cause unacceptable side effects, which makes vaccine development commercially risky. As a result, many promising vaccine candidates get stuck in the 'death valley' between early stage testing and large-scale trials.

This is especially true when it comes to developing vaccines against diseases that are endemic in low-income countries with restricted healthcare budgets. The global health community could pull policy levers to shift the financial



In the vaccine community, we don't look for barriers. We look for ways of getting things done



Dr Stephen Lockhart, Pfizer

incentives for pharmaceutical companies and their shareholders, encouraging investment and innovation in vaccine development.

Delivering vaccines to everyone who needs them

While it is essential to push forward with the development of new vaccines, we should not forget the ones we already have. Global infant vaccination rates have been stuck at around 85% for the past ten years with factors such as war, unstable political situations and poverty limiting healthcare access for the remaining 15% of children.

Bringing immunisation to low-income settings raises many challenges: where are the people who will benefit the most, and which diseases do they need protection from? Can vaccines be manufactured in a cost-effective way, then shipped to the communities that need them without the need for refrigeration? And are there enough trained healthcare workers to deliver them when they arrive? Solving these problems will be a crucial part of improving global public health.

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These genetic technologies should be put to use in the next generation of vaccines, making them cheaper and more accessible to people wherever they need it

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Professor Beate Kampmann,
IMPRINT Network

The future is now

Exciting things are coming in the world of vaccine research. Aside from COVID-19, which is currently dominating international research efforts, one of the next vaccines that is expected to come to market soon is for respiratory syncytial virus (RSV) – a development that could save the lives of tens of thousands children in the poorest parts of the world. Further into the future, there is hope for universal flu and broad-spectrum bacterial vaccines that work against current and future strains of these fast-evolving microbes.

One major hurdle is the speed at which vaccines make the journey from the lab to the clinic. This is particularly pressing in fast-spreading outbreak situations caused by emerging pathogens previously unknown to science. Novel technology platforms are creating the next generation of DNA or RNA vaccines based on the genetic code of the infectious agent. Unlike conventional immunisations, these vaccines can be put into production quickly and easily, potentially even in low-resource local settings.

However, all these innovations require investment. Since 2017, there has been a decrease in grants awarded each year by all top 10 funders of vaccine research and development in the UK (see page 8). If this continues, we are likely to lose our momentum and our ability to capitalise on the UK's position at the forefront on immunity research.

Case Study



Building on knowledge to accelerate progress

Peter Openshaw is Professor of Experimental Medicine at Imperial College London, and was president of the British Society for Immunology for five years. His research focuses on vaccines against flu and RSV.

“We can't be complacent. Every infectious disease is a many-headed hydra; you cut one off and three more pop up. We are trying to counter these microbial threats, but they constantly change and re-appear. Whenever you think you can sit back and take a breath, another one comes.

“There are still many unsolved questions and diseases for which we need new or better vaccines. But we don't start any vaccine development from ground zero. All the work that has been supported by organisations like the Wellcome Trust and the British Society for Immunology over the past many decades has laid the foundations for developing new vaccines when we need them.

“Making a vaccine from scratch can take 20 years or more but building on prior knowledge can accelerate the process, enabling us to get people immunised quickly when we need it. That was certainly the case for the recent Ebola vaccine and it is the same for the novel COVID-19 vaccines that are already entering clinical trials.”

The hunt for a COVID-19 vaccine

The COVID-19 pandemic has affected millions of people worldwide, creating a global health emergency. Researchers all over the world are racing to understand SARS-CoV-2, the coronavirus behind the disease, and find a safe and effective vaccine. At least two UK research groups have developed candidates that will soon enter clinical trials, but there is still plenty of work to do to protect the world's health.

The search for a vaccine

On 31 December 2019, health authorities in Wuhan, China, reported a cluster of patients with cases of pneumonia with an unknown cause to the WHO. The disease was eventually named COVID-19 and a novel coronavirus, SARS-CoV-2, identified as the virus behind it.

The virus rapidly spread, infecting millions worldwide in a matter of months. Many countries have introduced restrictive measures such as social distancing or lockdowns to contain or slow the spread, protect vulnerable populations and avoid overburdening healthcare services. Despite these efforts, protecting the population through widespread vaccination will be the only way to beat the disease in the long term.

By the end of March 2020 there were already more than 40 vaccine candidates in development from academic groups, established pharmaceutical companies and start-ups in many countries. This number had grown to at least 70 by the middle of April as more organisations joined the international research effort. Some are created from genetic material (RNA or DNA) derived from SARS-CoV-2, while others are based on fragments of its proteins.

A small number of vaccines are close to or have already started early-stage clinical trials where they are being evaluated for safety and effectiveness in small groups of volunteers. Ultimately, only one vaccine needs to succeed but having a wide field of potential candidates increases the chances that one or more will work.

Two UK COVID-19 vaccines in development

Scientists at the University of Oxford led by Professor Sarah Gilbert are developing a vaccine that uses a harmless weakened virus from chimpanzees to deliver coronavirus RNA into cells in the body. Once the cells receive the RNA they produce viral proteins, which stimulate the immune system to generate protective antibodies against future coronavirus infection.



The international research community has responded to COVID-19 at unprecedented speed. There has been incredible global cooperation



Dr John Tregoning, Imperial College London

Similar experimental vaccines have already been tested in early stage clinical trials against MERS (Middle East Respiratory Syndrome), proving that this technique is safe for use in humans. Clinical trials of the virus-based SARS-CoV-2 vaccine are starting in April 2020.

At Imperial College London, Professor Robin Shattock and his team are working on a more experimental 'plug and play' approach, creating a vaccine made from self-amplifying RNA encapsulated in tiny droplets.

This vaccine contains genetic instructions encoding both the virus spike protein (the part most likely to induce an immune response) and RNA copying machinery, enabling the vaccine to self-replicate inside cells and generate a greater protective immune response. The Imperial team expects to start clinical trials in June 2020.

When will the coronavirus vaccines be ready?

All of the vaccines in development must first prove they are safe and effective in small-scale clinical trials, which could take many months. Next come the challenges of scaling-up manufacturing and larger clinical trials involving hundreds or thousands of people before widespread rollout. This will be no small feat: vaccines are commercially risky investments

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A global vaccine is still unlikely before 2021, but we could see large-scale trials late in 2020”

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Dr John Tregoning, Imperial College London

for pharmaceutical companies and production facilities are generally designed to produce one specific vaccine. The scaling up of infrastructure to manufacture any new vaccine will be a very serious challenge.

There are still many questions about COVID-19 that need to be answered as we progress towards effective vaccine implementation: How long does immunity last and how many doses will be needed? Does protection vary between people according to genetic background, age or sex? And who should get priority access to vaccination in order to most effectively protect vulnerable populations?

Learning from this pandemic to prepare for the next

The response from the research community to COVID-19 has been impressive, but it has also highlighted that the world needs to be better prepared for the next pandemic, whatever it may be. There is an urgent need to support and fund global capabilities in immunology, modelling, diagnostics and vaccination against all infectious diseases - including the ones we don't even know about yet.

Typically, when infectious diseases fade from the headlines, the funding for research dries up too. If intensive research into coronavirus infections like SARS and MERS had continued in the wake of past outbreaks, we might have been better equipped for tackling COVID-19 today.

It is also essential not to overlook the impact that the pandemic will have on progress against the many other infectious diseases that still cause death and misery around the world. The disruption to healthcare infrastructure that currently delivers routine immunisation programmes for lethal childhood diseases like polio, typhoid and measles risks the lives of many thousands of children.

Case Study



New technology on trial

Professor Robin Shattock and his team at Imperial College London are building a 'plug and play' vaccine development platform, with the aim of rapidly producing novel RNA vaccines against emerging diseases based on their genetic code. The COVID-19 pandemic is the first real test of this technology, and progress has been incredibly fast.

"We were able to go from having the virus' genetic code to building a prototype vaccine and our first animal experiments within three weeks. In animals, the vaccine induced very potent neutralizing antibodies with a single immunisation," says Shattock.

Crucially, the Imperial team's RNA-based vaccine amplifies itself in the body, giving it a unique advantage over other candidates when it comes to manufacturing. "We can use very low doses of RNA in the self-amplifying vaccine, so we can make a million doses in a litre of reaction material," he explains.

Shattock thinks the simplicity of this genetic platform approach, combined with relatively easy scale-up and manufacturing, will play a central role in providing vaccines for existing diseases and future outbreaks. "We could build networked vaccine manufacturing platforms around the world. So if another pandemic occurs, everyone could make a vaccine for their local population, instead of waiting for centralized production. We're not there yet, but that is the vision."

Protecting the health of the world

We have made huge progress from the early days of Jenner and his cowpox pustules to the latest high-tech vaccine development platforms. Today, vaccines save millions of lives around the world every year, and prevent many more people from suffering debilitating diseases, but there is much more that can be achieved as long as the current momentum is sustained.

There are high hopes that we might soon be able to eradicate diseases like polio, rubella and measles with the vaccines we already have. Ensuring truly global access to immunisation programmes would make a big difference to child mortality in some of the poorest and most unstable parts of the world. However, this is heavily dependent on political willpower, funding for vaccine delivery and access to healthcare.

There have also been notable recent successes with novel vaccines against diseases such as Ebola and typhoid, with respiratory syncytial virus (RSV) coming close behind. At the moment there is an impressive global effort going towards finding vaccines that can provide protection against SARS-CoV-2, the coronavirus responsible for COVID-19.

The reliability and effectiveness of vaccines means that they easily can be taken for granted as a public health intervention. Many vaccine-preventable diseases are little more than distant memories in wealthier countries, and it can be particularly hard to maintain vaccination rates when the prevalence of a disease is low. A decrease in vaccine uptake has allowed once rare diseases to re-emerge within the UK, as we have seen with measles recently, and which led the UK to lose its WHO 'measles free' status in August 2019. Public engagement therefore plays a vital role in maintaining the life-saving reputation of vaccines, as well as ensuring support and funding for future research.

One thing is clear: vaccines transform societies all over the world. Only clean drinking water is a more effective public health measure. Preventing children from dying from infectious diseases, suffering long-term side effects or missing school due to illness helps to build a healthy, educated population. In turn, this decreases the emotional, practical and financial burden on families, significantly reducing individual and national healthcare costs.

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The COVID-19 pandemic teaches us that protecting against infectious diseases isn't just about defending health and saving lives: it's about the global economy, freedom and security. We all need to pull together - the health of the world is at stake

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Professor Andrew Pollard, University of Oxford

However, the opposite is also true. New pathogens can quickly spread through our interconnected world, rapidly destabilising society with dramatic personal, economic and political impacts. We must learn to work smarter and faster, gathering data on outbreaks as they spread, analysing the genetic makeup of pathogens and immune responses, and bringing new vaccines into clinical trials as quickly as possible. UK researchers are standing shoulder to shoulder with our international colleagues to address these challenges and protect the health of the world.

Thank you

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More information on this report, including a list of references, can be found on the British Society for Immunology's Celebrate Vaccines website. Visit www.celebratevaccines.com/policy for more information.

The British Society for Immunology's mission is to promote excellence in immunological research, scholarship and clinical practice in order to improve human and animal health.



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