Vaccines Europe pipeline review 2023 – UK edition

Innovating for tomorrow, today

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Vaccines Europe

Contents

ABOUT THIS REPORT

This report is an adaptation of the Vaccines Europe Pipeline Review 2023, which aims to present pipeline information within a specific UK policy context. The UK edition has been developed jointly by Vaccines Europe and the Association of the British Pharmaceutical Industry.

Foreword

Vaccines represent an important symbol of progress in science and technology in the past decades.

They are complex medicinal products tailored to provide protection against specific infectious diseases and, therefore, improve the overall well-being of populations and contribute to the development of resilient healthcare systems. Developing successful vaccines is not an easy task and it is thanks to countless dedicated individuals in the scientific community that a wide range of vaccines are available today, protecting all of us against many life-threatening diseases. The field is evolving at great speed. Many promising vaccines enter the market every year and many more are being developed, with the end goal of saving as many lives as possible from dangerous infectious diseases.

Looking at the challenges ahead of us, such as climate change, antimicrobial resistance, ageing populations, zoonoses and the geographic spread of vectors carrying infectious diseases, it is important to build on the successes of the past and to ensure an environment supportive of innovative immunisation. While vaccines alone cannot solve any of these challenges, they have been proven to provide significant support in addressing them.

Vaccine innovation is important, but equally important is where it happens. The government's Life Sciences Vision included a commitment to "sustain the UK position in novel vaccine discovery, development, manufacture and use of vaccines" and in recent years several steps have been taken that should help to strengthen the national vaccine ecosystem.[1] But the pathway to adopting an innovative vaccine into the UK national immunisation programme - particularly where there is no existing programme for that disease or target population - remains complex, lengthy and uncertain.

Vaccine manufacturers remain committed to playing their part in ensuring a healthier tomorrow for the entire population. But the complexity of these upcoming threats is very high and requires a concerted effort from all stakeholders.

Sibilia Quilici
Executive Director, Vaccines Europe

Amit Aggarwal
Executive Director Medical Affairs and Strategic Partnerships, ABPI

Introduction

Vaccination has been a transformative tool in society over the last century, leading to the almost complete eradication of diseases with high levels of morbidity and mortality. In so doing, vaccines have saved countless lives and prevented many long-term health complications and disabilities caused by various pathogens. Vaccination has also been critical in combatting emerging infectious diseases and outbreaks, such as the H1N1 influenza pandemic in 2009 or the more recent COVID-19 pandemic, and it is a key contributor in the fight against vaccine-preventable cancers. Data presented by World Health Organization (WHO) at the European Congress of Clinical Microbiology & Infectious Diseases (ECCMID) in April 2023 shows that COVID-19 vaccination directly saved approximately one million lives across Europe between December 2020 and March 2023,[2] proving the value vaccines bring to society at large.

Today, vaccine innovation and vaccination continue to play a significant role in public health and increasing the efficiency of healthcare, contributing to socio-economic advances and equity, as well as improving people's quality of life. While existing vaccines are key to overcoming some major challenges, there are still many more threats ahead. Innovation in vaccinology will be instrumental in addressing them.

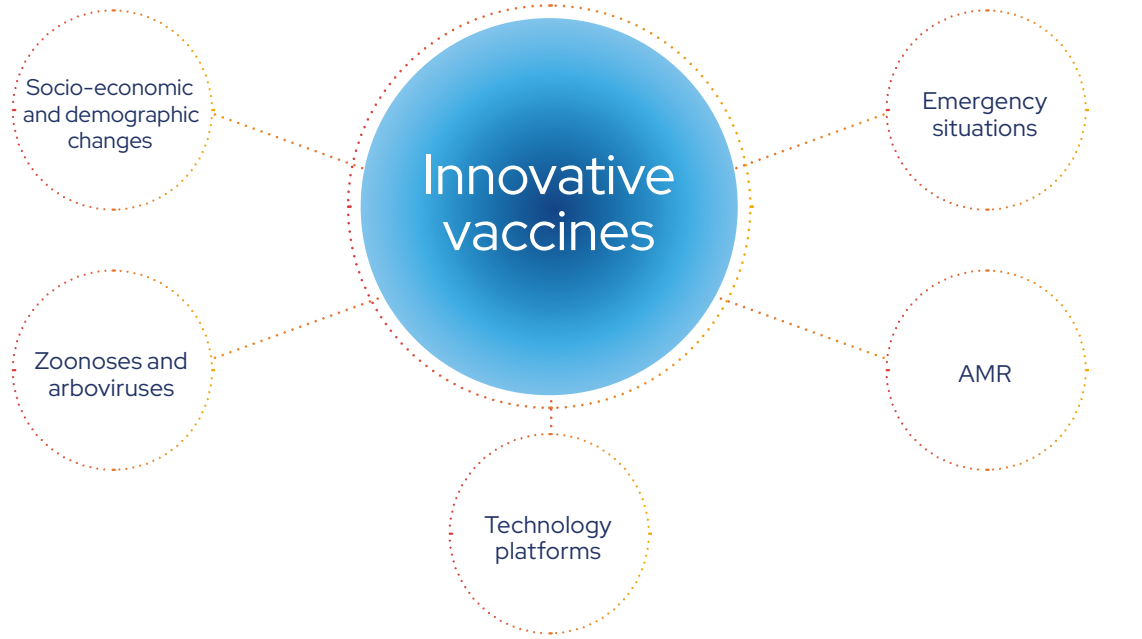
One of the biggest challenges now and in the future is antimicrobial resistance (AMR), which is projected to cause 10 million deaths annually by 2050, with global costs rising to over $1 trillion per year by 2050.[3,4] Vaccines have been recognised as cost-effective tools to prevent communicable diseases in humans and animals, with potential to curb the spread of AMR infections.[5]

The H1N1 and COVID-19 pandemics, as well as the recent signals from the scientific communities regarding the increasing risks of mosquito-borne diseases in Europe, such as chikungunya, dengue, Zika, yellow fever and West Nile fever,[6] remind us of the huge impact climate change could have on public health. Failing to protect the environment would make it easier for infectious diseases to emerge and spread to regions previously unaffected. This provides a stark reminder of the importance of taking a One Health approach to address these challenges, as the health of humans, animals and the environment cannot be separated from one another.

> Vaccine innovation and vaccination continue to play a significant role in public health, increasing the efficiency of healthcare, contributing to socio-economic advancements, and improving people's quality of life.

The COVID-19 pandemic also underscored the importance of protecting all members of society, regardless of their age, gender, status or geographical location. The lessons should be further incorporated into national and European immunisation strategies to reflect the importance of vaccination throughout one's entire lifespan and as a routine practice – not just in times of crisis.

Recent decades witnessed impressive developments in the vaccine ecosystem, but many unknowns and challenges remain. Innovation and cross-sectoral collaborations are essential to addressing the global challenges of today and tomorrow and to create healthier lives for everyone, by:



- developing vaccines to respond to the socio-economic and demographic changes in Europe and to help build resilient healthcare systems, such as vaccines against respiratory syncytial virus (RSV), group B *Streptococcus* and influenza infections
- developing vaccines for emergency situations,[7] like COVID-19, Middle East respiratory syndrome (MERS), Zika virus infection, Nipah virus infection, and henipaviral diseases
- developing travel and endemic vaccines for zoonoses or arboviruses, such as dengue fever, chikungunya virus, malaria, yellow fever and rabies
- developing vaccines to slow the emergence and spread of drug-resistant bacteria, such as *Clostridioides difficile*, *Shigella* spp., *Escherichia coli*, *Neisseria gonorrhoeae*, *Salmonellae* and *Streptococcus pneumoniae*
- developing vaccines to help protect against and treat different types of infection-associated cancers, such as those against hepatitis B, human papilloma virus (HPV), Epstein-Barr virus (EBV) and glioblastoma (Cytomegalovirus-positive)
- developing therapeutics that utilise vaccine technology to treat diseases caused by infectious agents such as hepatitis B and herpes simplex virus

Through innovation we can support the diversification of vaccines, providing prescribers with options that enable them to meet people's needs more closely. Diversification of platforms also ensures supply reliability, decreasing the risk of shortages as well as vaccine introduction delays, and encourages competition to continue driving innovation.

What's in this report?

Vaccines Europe conducted the first ever pipeline review of its 15 member companies[8] in 2022.[9] The current edition represents an updated version of the report with data from July 2022 to August 2023 and incorporates feedback received from several key stakeholders, such as DG HERA*, EMA**, EDQM*** and the University of Perugia Of note is the change in membership within Vaccines Europe, with one company leaving and a new one joining, which slightly influences the data presented compared to 2022. Publicly available information was collected and classified based on a range of criteria. The data was analysed to highlight current trends in the research and development of vaccines, as well as how the vaccine industry helps to address the challenges of tomorrow. Preclinical development was excluded from this analysis. The report aims to present the research trends of Vaccines Europe members in an aggregated manner and therefore no information pointing towards specific companies is provided (such as vaccine candidate names or references to the clinical trials). While for some products the expected timelines for data submission to regulatory agencies can be found in the public domain, this information was excluded from the pipeline review as it refers to individual products and is part of companies' internal strategies.

The report aims to raise awareness of the importance of innovation in the vaccine ecosystem and to showcase the commitment of vaccine manufacturers to reducing preventable public health threats, saving millions of lives globally and contributing to healthcare and socio-economic resilience. We hope that this report can serve as a first step for national horizon-scanning activities in all European countries, as well as a basis for early discussions between vaccine developers and health authorities on topics such as value assessment of vaccines, immunisation financing and country readiness. The report is structured around key topics that represent challenges in the healthcare and health policy fields. Under each section, examples of vaccine candidates from the pipeline of Vaccines Europe members can be found. It should be noted, however, that some vaccine candidates could fit under multiple sections. For an overview of the challenges that could potentially be addressed by these vaccine candidates, labels have been added next to each candidate, according to the following legend:

- AMR — Antimicrobial resistance
- CR — Infection-associated cancer vaccines
- CC — Climate change
- MI — Maternal immunisation
- RI — Routine immunisation (including vaccines that could potentially be administered routinely in the future)
- ThV — Therapeutic vaccines
- TrV — Travel vaccines
- UPHN — Unmet public health needs (Diseases for which there was no vaccine on the market by the end of July 2023)
- ZOO — Zoonoses

* Health Emergency Preparedness and Response Authority
** European Medicines Agency
*** European Directorate for the Quality of Medicines & HealthCare

By the end of August 2023, there were 103 vaccine candidates in the pipeline, of which 99 were prophylactic vaccines and four were therapeutic vaccines (targeting infectious agents). Most of the vaccine candidates target infectious diseases caused by viruses, but there are also a significant number targeting bacteria-induced infections. There are also two vaccine candidates against Plasmodium, the parasite causing malaria.

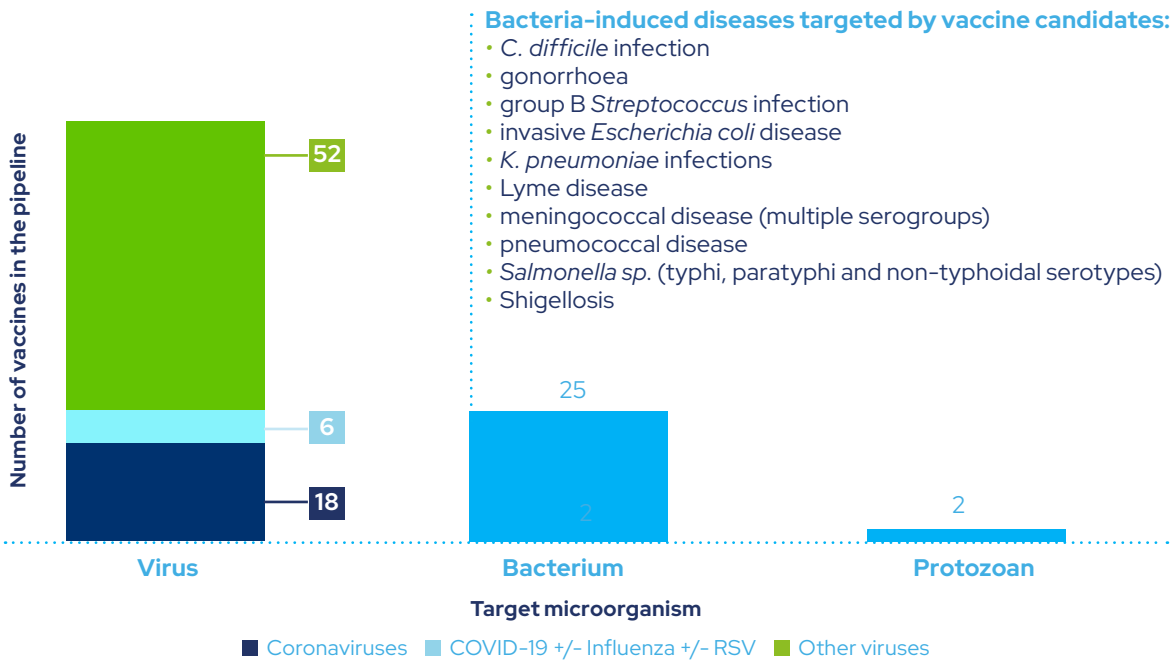
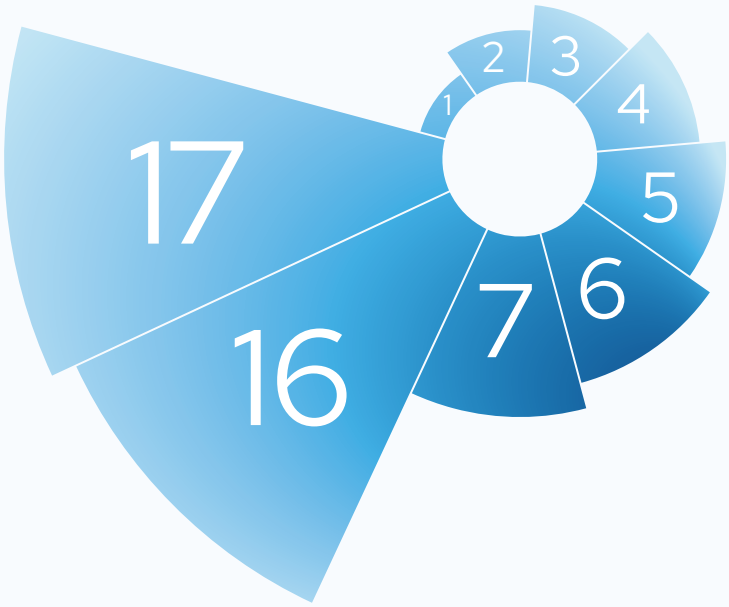


Figure 1. Number of vaccines in the pipeline targeting a specific type of microorganism.

The most frequent targets for vaccine candidates were COVID-19 (SARS-CoV-2) (18 candidates, including in combination with other coronaviruses), followed by influenza (16 candidates), meningococcal disease (seveen candidates) + RSV (six candidates). On top of these, several vaccine candidates are designed to target a combination of these viruses (three candidates against COVID-19 + influenza, one candidate against COVID-19 + influenza + RSV, one candidate against COVID-19 + RSV and two candidates against influenza + RSV). The full overview of the vaccine candidates of Vaccines Europe member companies can be consulted in Figure 2.



1 vaccine candidate

- Chikungunya virus
- COVID-19 + influenza + RSV
- COVID-19 + RSV
- COVID-19 + other coronaviruses
- Dengue fever
- Invasive *Escherichia coli* disease
- Glioblastoma (via CMV)*
- Gonorrhoea
- Group B streptococcus infection
- HPV
- Human metapneumovirus and RSV (hMPV/RSV)
- Influenza (pandemic)
- *Klebsiella pneumoniae*
- Measles, mumps, rubella, varicella
- Nipah virus
- Norovirus
- Shigellosis
- Shingles
- Yellow fever

2 vaccine candidates

- Epstein-Barr virus infection (EBV)
- Hepatitis B*
- Herpes simplex virus*
- HIV
- Influenza + RSV
- Lyme disease
- Malaria
- Rabies
- *Salmonella sp.*
- Varicella

3 vaccine candidates

- COVID-19 and Influenza
- Cytomegalovirus (CMV)
- Zika

4 vaccine candidates

- Clostridioides difficile infection

5 vaccine candidates

- Pneumococcal disease

6 vaccine candidates

- Respiratory syncytial virus

7 vaccine candidates

- Meningococcal disease

16 vaccine candidates

- Influenza

17 vaccine candidates

- COVID-19 (different strains)

*Therapeutic vaccine

Figure 2. Number of vaccine candidates addressing a disease area.

All stages of clinical development are well represented in the pipelines of Vaccines Europe members. At the end of August 2023, there were 25 vaccine candidates in Phase III of the clinical trials and seven under review by a regulatory agency. A summary of the vaccines organised by their status of development can be consulted in Annex I.

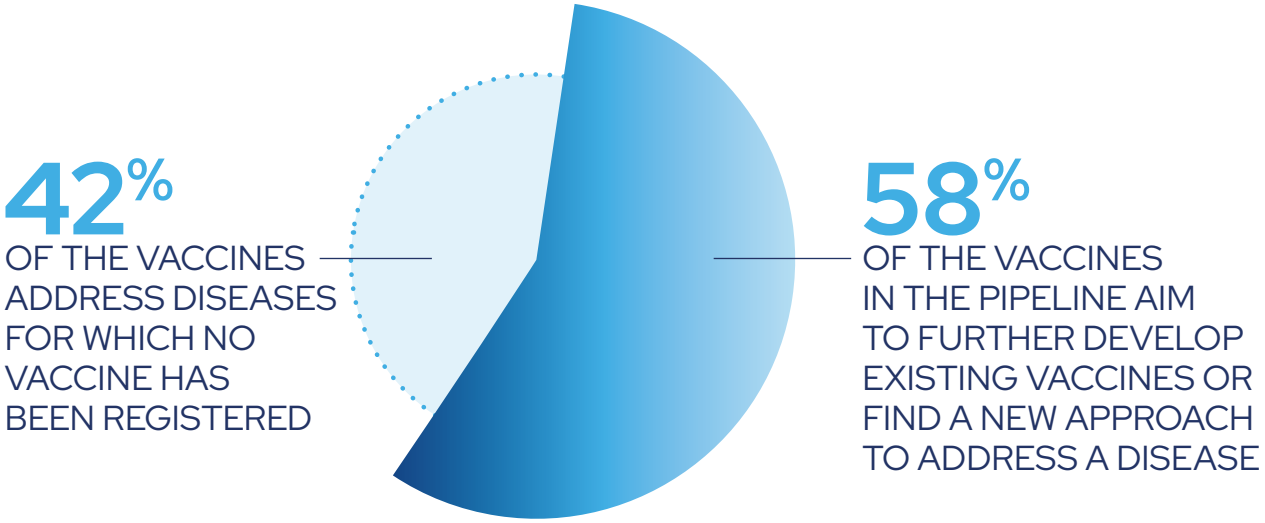


Figure 3. Percentage of vaccines targeting diseases for which there are no registered vaccines vs those further developing existing products.*

42% of the vaccine candidates in our members' pipelines aim to address diseases (or a combination of diseases) for which no vaccine has been registered until now:

- Chikungunya virus infection
- *Clostridiodes difficile (C. difficile)* infection
- COVID-19 + influenza
- COVID-19 + influenza + respiratory syncytial virus
- COVID-19 + respiratory syncytial virus
- cytomegalovirus infection
- Epstein-Barr virus infection
- gonorrhoea
- glioblastoma (via Cytomegalovirus)
- group B *Streptococcus* infection
- hepatitis B – therapeutic use
- *herpes simplex* virus infection
- human immunodeficiency virus (HIV) infection
- human metapneumovirus and respiratory syncytial virus
- influenza + respiratory syncytial Virus
- invasive *Escherichia coli* disease
- *Klebsiella pneumoniae* infection
- *Borrelia burgdorferi* (Lyme disease)
- meningococcal disease (vaccines targeting 5 serogroups - A, B, C, W, Y)
- norovirus
- nipah virus
- respiratory syncytial virus – paediatric use
- *Shigella* spp. (Shigellosis)
- Zika virus

* Note: for therapeutic candidates for which there is a preventative vaccine licensed, the answer was marked 'no'. The answer has also been marked 'no' for candidates for which a vaccine is licensed for a different age group (e.g., RSV), for individual pathogens, but not in combination (e.g., COVID-19 + influenza) or for candidates including serogroups not present in the existing product (e.g., meningococcal ABCWY disease).

RI Routine immunisation

UPHN Unmet public health needs

	POPULATION	STATUS	PLATFORM
CYTOMEGALOVIRUS (CMV)[10,11,12] • Cytomegalovirus (CMV) is a common virus for people of all ages, affecting the eyes, lungs, liver, oesophagus, stomach, and intestines of people with weakened immune systems. • ~60% of adults in developed countries and more than 90% in developing countries infected. • Babies born with congenital CMV infection could lose their hearing and may suffer other developmental disabilities.[13] • In the US, nearly one in three children infected by age five. • Currently, no vaccine available to prevent congenital CMV. **Vaccines in the pipeline: 3**	Adults (3)	Phase I (2) Phase III (1)	Protein subunit (1) mRNA (1) Virus-like particle (1)
HUMAN IMMUNODEFICIENCY VIRUS (HIV)[14] • Major global public health issue, having claimed 40.4 million lives so far. • Attacks the body's immune system, weakening a person's immunity against opportunistic infections (tuberculosis, fungal infections, severe bacterial infections, and some cancers). • 39.0 million people living with HIV at the end of 2022. 630,000 deaths in 2022. • No cure for HIV infection but a manageable chronic health condition. **Vaccines in the pipeline: 2**	Adults (2)	Phase I (2)	mRNA (2)
NOROVIRUS[15,16] • Highly contagious infection that can cause vomiting, diarrhoea, and stomach pain, resulting in fluid loss. • As immunity may only last a few months and is strain-specific, and given their genetic variability, infection can happen several times in a lifetime and affects individuals of all ages. • Causes approximately 685 million cases annually. Of those, around 200 million cases are seen among children under 5 years old, leading to an estimated 50,000 child deaths every year. **Vaccines in the pipeline: 1**	Adults (1)	Phase I (1)	mRNA (1)

Vaccine innovation also involves further developing vaccines that have been available to the population for years or finding new approaches to address a disease area. We refer to this as incremental innovation.

58% of vaccine candidates aim to address the disease areas for which there are already existing vaccines by:

- improving formulations to increase the convenience for healthcare professionals and patients
- expanding a vaccine's use to a new population
- including more target strains in a vaccine
- developing combination vaccines, which could decrease the number of injections and better fit with national vaccination schedules
- using a new approach to address a disease (e.g., using a different technology platform, targeting a different part of the antigen)

While all authorised vaccines are generally well tolerated and effective, Vaccines Europe members are continuously working to improve the knowledge of vaccines' benefits/risks as part of their post-authorisation lifecycle development.

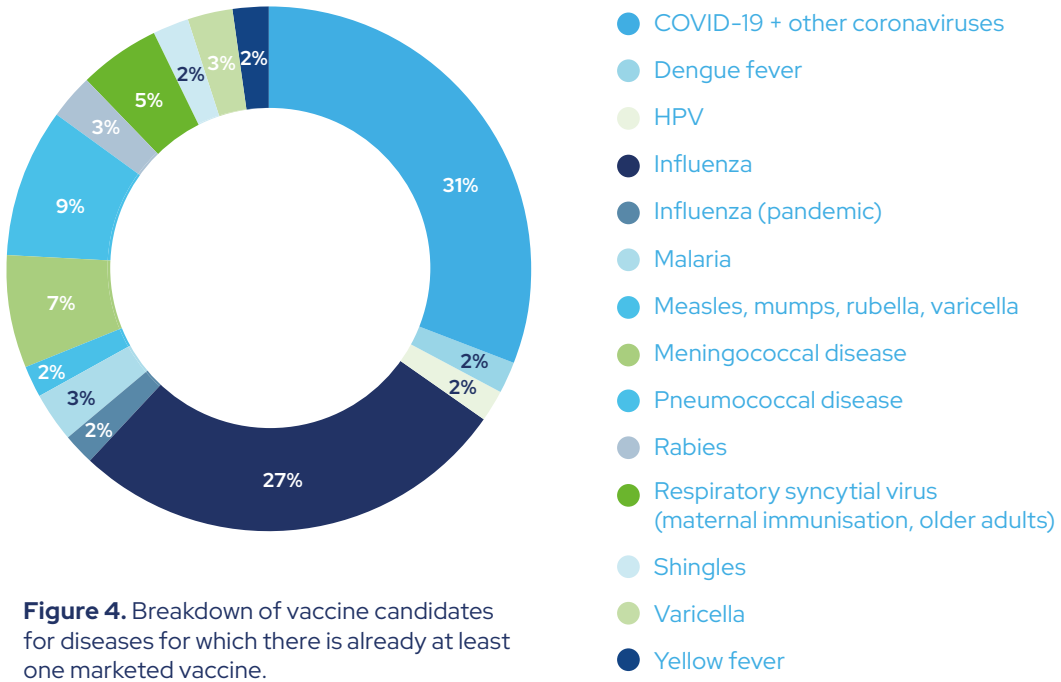


Figure 4. Breakdown of vaccine candidates for diseases for which there is already at least one marketed vaccine.

A constantly evolving research environment

The research environment for vaccines is very dynamic, evolving constantly to address emerging infectious diseases that affect people across different regions. Vaccine development is complex, usually taking 10 to 15 years,[17] with costs varying between $0.5 billion and $1 billion USD.[18]

Clinical trials are a big part of the development of new vaccines. For candidate vaccines, these rigorous studies aim to assess the efficacy and safety of a product in otherwise healthy populations. The performance and safety of the candidates are reviewed after each clinical trial stage. While some candidates will progress to the next development step, others will be discontinued for various reasons, such as suboptimal immune response or safety concerns. However, the results of clinical trials are not the only factors that could stop the progression of candidate vaccines. There are many other challenges that research-based companies encounter at this stage, such as:

- complexities of recruiting and retaining a diverse and representative group of participants, especially when it comes to long-term follow-up to assess duration of protection
- logistical challenges, especially for multi-site trials
- resource constraints: funding, research infrastructure, trained personnel
- evolving epidemiology, including the emergence or disappearance of variants, strains, and pathogens

Besides the challenges related to conducting clinical trials, there are other complexities vaccine manufacturers must overcome in order to bring successful candidates to the market, such as:

- bridging the gaps in scientific knowledge: fully understanding the structure of specific pathogens, how they replicate and spread as well as pathogen-host interactions is critical to selecting the appropriate antigen and developing effective candidates
- designing candidates that provide protection across a diverse population with variability in immune responses
- ensuring a continuous cold chain from production to administration, especially in areas with limited resources and/or very high temperatures
- funding beyond preclinical and clinical development, to ensure manufacturing scale up and wide distribution of the product

In spite of all these challenges, the vaccine research ecosystem is constantly developing and adjusting to match the needs of populations. Additionally, new human vaccine players born out of the pandemic are becoming more present in this ecosystem.

Thirteen of the vaccine candidates reported in the 2022 pipeline review were granted Marketing authorisation by at least one regulator before the end of August 2023. During the same period, 18 candidates progressed to the next development stage, while 16 development programmes werediscontinued. Thirty-nine new candidates have been included in the pipelines of Vaccines Europe (VE) member companies. The therapeutic candidates that do not target infectious agents have no longer been included in the 2023 pipeline review. However, several products developed as monoclonal antibodies for prophylactic use have been included to reflect the current trends.

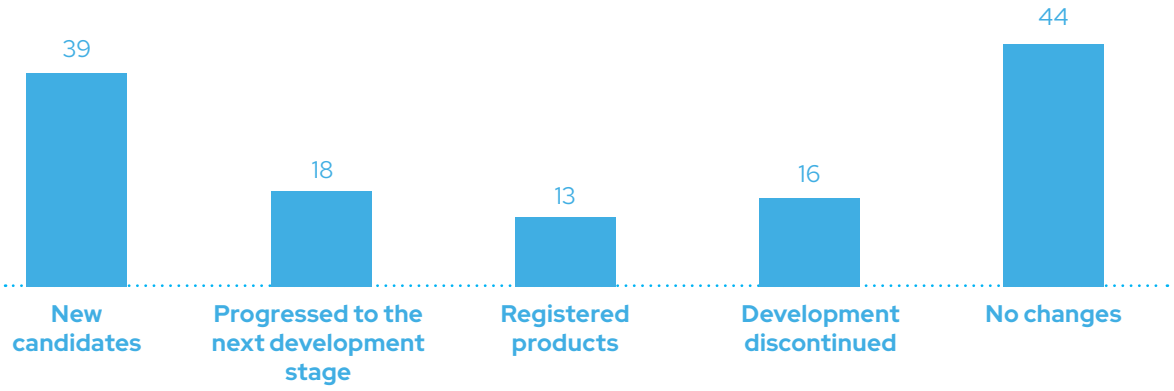


Figure 5a. Updates in the pipelines of VE member companies since July 2022

NUMBER OF CANDIDATES	CHANGE COMPARED TO PREVIOUS PIPELINE REVIEW	DISEASE AREAS
13	Marketing authorisation granted	COVID-19, dengue fever, Ebola and RSV.
18	Progress to the next development stage	COVID-19, herpes simplex virus, influenza, pneumococcal disease, RSV, Zika virus infection.
39	New candidates	*C. difficile* infection, COVID-19 +/- influenza +/- RSV, dengue fever, Epstein-Barr virus infection, gonorrhoea, herpes simplex virus, HPV, human metapneumovirus and RSV, influenza, influenza + RSV, pandemic flu, Lyme disease, MMRV, pneumococcal disease, meningococcal disease, RSV, Salmonellae (typhi, paratyphi, non-typhoid), shigellosis, shingles, varicella
16	Development discontinued	Chikungunya virus, cytomegalovirus, COVID-19 +/- influenza, Ebola, HIV, human metapneumovirus and parainfluenza virus 3, pneumococcal disease, RSV, shigellosis, and skin and soft tissue infection caused by *S. aureus*.

Figure 5b. Updates in the pipelines of VE member companies between July 2022 and August 2023.

Cross-sectoral collaborations and partnerships play a critical role in vaccine development. These either provide funding for promising candidates to enable progress through costly development stages, or leverage knowledge and other resources from various stakeholders to enhance scientific understanding and accelerate the development process. Vaccines Europe members are partnering with a wide range of private and public stakeholders to advance their candidates. Examples include but are not limited to: Bill and Melinda Gates Foundation, universities, National Institutes of Health, the US Biomedical Advanced Research and Development Authority, the National Institute of Allergy and Infectious Diseases, the International AIDS Vaccine Initiative, Government of Canada and the Coalition for Epidemic Preparedness Innovations.

Protecting the health of our society

The vaccines that are currently in the pipeline cover different types of populations across the lifespan. However, 83 of them are tested in adults and older adults, reflecting the challenges related to ageing populations and the need for a paradigm shift towards a life-course approach to vaccination.

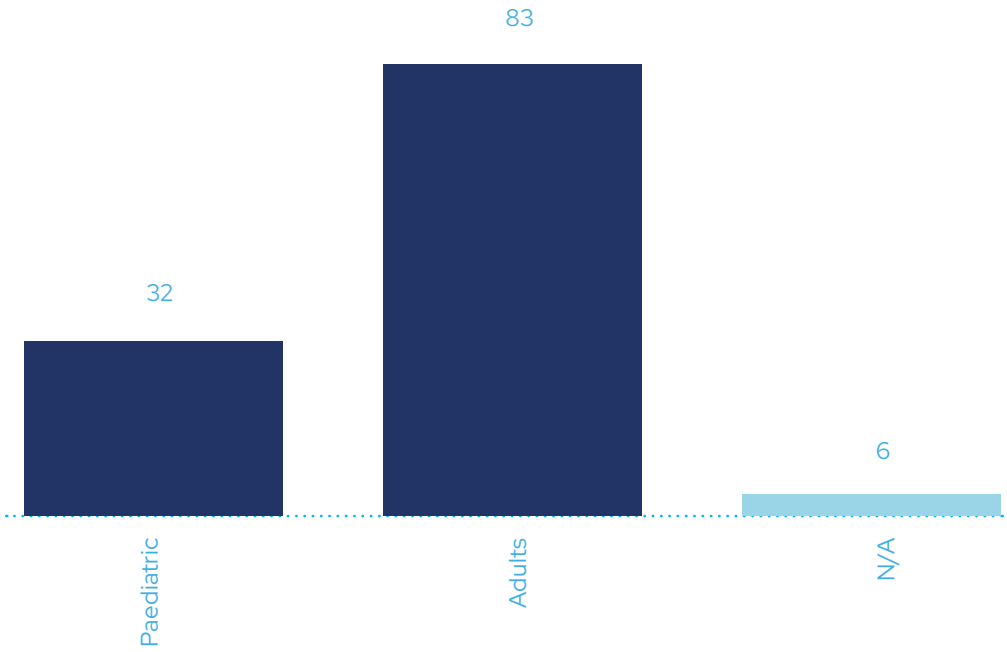


Figure 6a. The number of vaccine candidates tested in each type of population*.

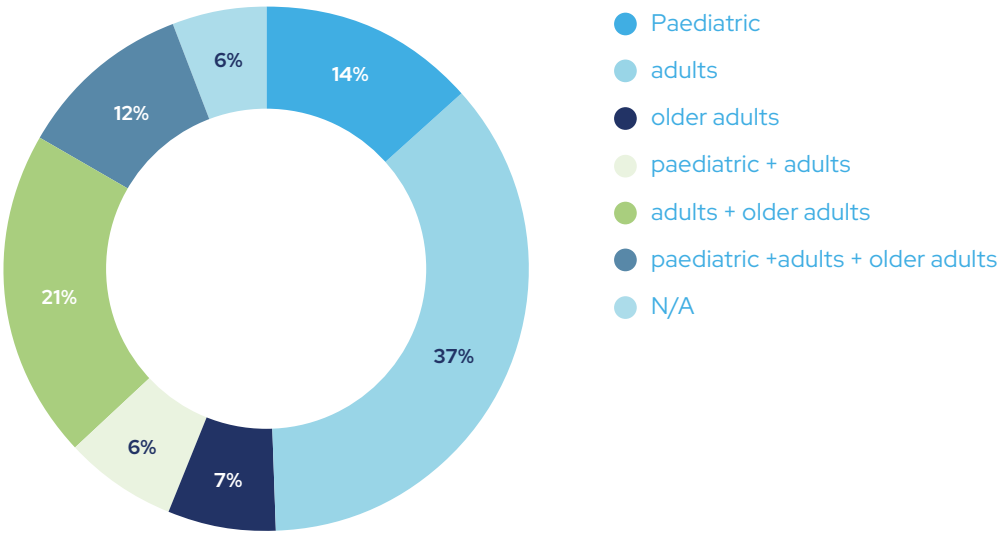


Figure 6b. The number of vaccine candidates tested in each type of population.

*Some of the candidates are tested in multiple populations and therefore have been counted multiple times.

ROUTINE VACCINES ACROSS THE LIFESPAN

The life-course approach to vaccination means protecting people at all stages of life. This includes infants, children, adolescents, adults, older adults, pregnant women, people with comorbidities, and immunocompromised individuals.

Childhood vaccination is one of the greatest medical success stories of the 20th century. However, infectious diseases can also have a devastating impact on adults' health, due to the decline of the immune system, which makes them more susceptible to infectious diseases. The UK's population is ageing - in 1999 one in six people were aged 65 years and over; this increased to one in every five people in 2019 and is projected to reach around one in every four people by 2039.[19] While the UK has several established adult immunisation programmes, vaccination coverage rates are generally lower than for paediatric programmes.

The COVID-19 pandemic has reinforced that adult immunisation is essential to protect adults against current and future vaccine-preventable diseases, drive socio-economic prosperity and equity and help mitigate potential public health crises. The need to extend the benefits of vaccination, from childhood alone to the entire lifespan, aligns with the increased role prevention plays in healthcare systems. To achieve this goal, better policies and funding allocation are needed to ensure adequate coverage rates for adults.[20]

There are currently 38 vaccine candidates for routine immunisation[21] in our members' pipelines, against influenza, varicella, HPV, measles, mumps, rubella, varicella (MMRV combination vaccine), and pneumococcal and meningococcal diseases.

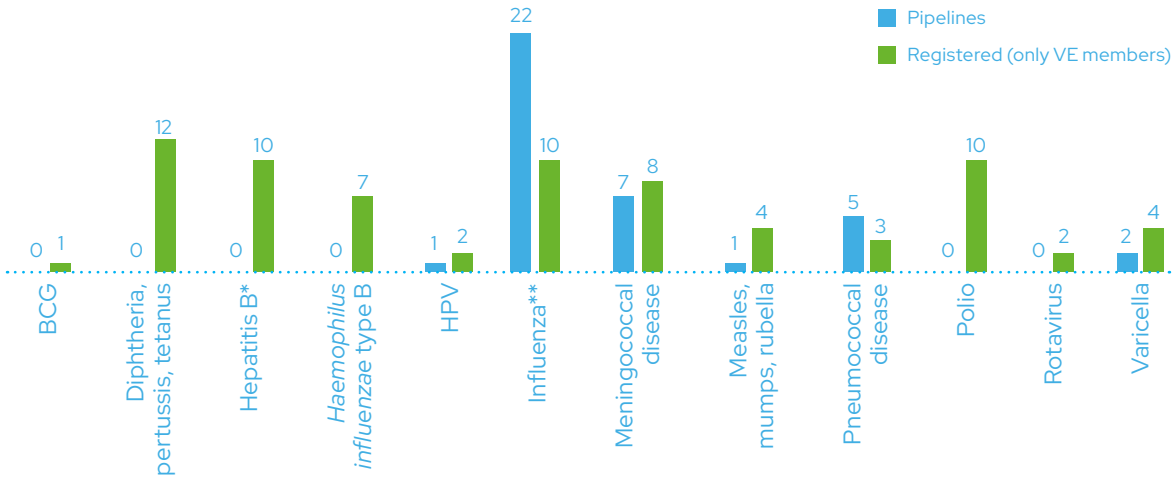


Figure 7. Vaccines in the VE members' pipeline for routine immunisation

*There are two vaccine candidates against hepatitis B in the pipeline, however they are intended for therapeutic use and therefore have not been included in this figure.

** The 22 influenza candidates include combinations with SARS-CoV-2 and/or RSV

Some of them are tested in both paediatric and adult populations. Routine immunisation refers to vaccinations recommended for defined eligible individuals at national or subnational level. In our analysis on routine immunisation, diseases relevant for the European region have been selected.

Respiratory infections responsible for sick leave, hospitalisation and death are a key challenge in the adult population. For example, seasonal influenza is a significant public health issue. In the UK the influenza season is associated with an increased demand for and pressure on the NHS and the loss of an estimated 4.8 million working days annually.[22] It is estimated that yearly seasonal influenza vaccination can save between €248 million and €332 million in healthcare costs in Europe by avoiding hospitalisations and visits to general practitioners.[23, 24]

Another example is RSV, which causes on average 213,000 annual hospitalisations in children under five years and 158,000 annual hospitalisations in adults in the EU, Norway and the United Kingdom.[25] Modelling data considered by the Joint Committee for Vaccination and Immunisation estimated that an RSV vaccination programme for people aged 75 and over in the UK could prevent 36,000 GP consultations, 4,600 hospitalisations, 1,000 ICU admissions and between 300 and 2,800 deaths each year.[26]

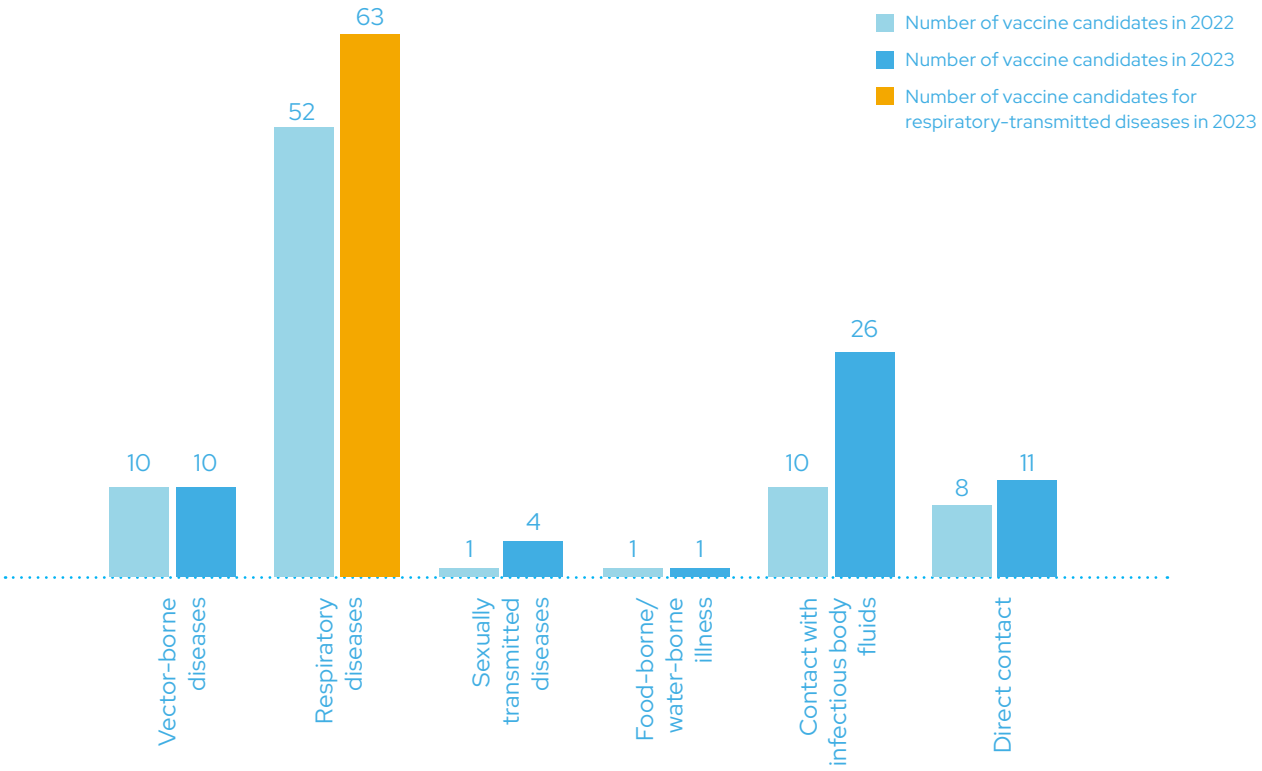


Figure 8. Number of vaccines in development by disease transmission route.

*The comparison with 2022 data is approximate as in 2022 the pathogens spreading through multiple routes have been counted separately, while in 2023 there are counted multiple times, under each section.

Vaccination has already contributed massively to reducing infant morbidity and mortality worldwide, but more can still be done by using maternal immunisation. For this approach, pregnant women are vaccinated, then the induced antibodies are transferred from mother to foetus through the placenta during pregnancy, or after birth in breast milk, providing protection against infections in the first few months of life. Our members' pipelines contain vaccine candidates for maternal immunisation against group B *Streptococcus* infections.

AMR Antimicrobial resistance · MI Maternal immunisation · RI Routine immunisation · TrV Travel vaccines · ZOO Zoonoses

	POPULATION	STATUS	PLATFORM
GROUP B *STREPTOCOCCUS* INFECTION (STREP B)[27] • Strep B bacteria can cause many types of infections, such as bacteraemia and sepsis, bone and joint infections, meningitis, pneumonia and skin and soft-tissue infections. • Strep B can cause long-term problems, such as deafness and developmental disabilities in babies. • 2 to 3 in every 50 babies (4% to 6%) who develop strep B disease die. • On average, about 1 in 20 non-pregnant adults with serious strep B infections dies. • Currently no licensed vaccine for the prevention of strep B. **Vaccines in the pipeline: 1**	Adult (1)	Phase II (1)	Glycoconjugate vaccine (1)
INFLUENZA[28, 29, 30] • Influenza virus types A and B are both common causes of acute respiratory illnesses. • Annual epidemics result in 3 to 5 million cases of severe illness and 290,000 to 650,000 respiratory deaths worldwide every year. • Severe morbidity and mortality more common among elderly people and in specific high-risk groups. • Influenza viruses undergo frequent changes in their surface antigens, with new influenza outbreaks occurring every year. • When a new flu A virus emerges to which most of the population does not have immunity and is spreading from individual to individual in an efficient and sustained way, a flu pandemic emerges. **Vaccines in the pipeline: 16 (influenza) + 2 (influenza + RSV) + 3 (influenza + COVID-19) + 1 (influenza + COVID-19 + RSV) + 1 (pandemic influenza)**	Paediatric (1) Adults (7) Adults + older adults (8) Older adults (2) Paediatric + adults + older adults (3) N/A (1)	Phase I (8) Phase II (8) Phase III (4) Under review (3)	Protein nanoparticles (2) mRNA (15) Whole-inactivated virus (5) N/A (1)
MENINGOCOCCAL DISEASE[31, 32, 33] • Caused by various serogroups of *Neisseria meningitidis*, which is one of the most common causes of bacterial meningitis in the world and the only bacterium capable of generating large epidemics of meningitis. • At least 12 serogroups of meningococcus have been characterised; five serogroups cause most of the cases worldwide (A, B, C, W, Y). • In 2018, more than 3,200 confirmed cases of invasive meningococcal disease (IMD), including 324 deaths, reported in 30 EU/EEA countries. • Often a rapid progression of the disease, with an 8-15% case-fatality ratio. This may result in death within one or two days after onset of symptoms. **Vaccines in the pipeline: 7***	Paediatric (4) Paediatric + adults (1) Paediatric + adults + older adults (1) N/A (1)	Phase II (3) Phase III (3) Under review (1)	Protein subunit (2) Glycoconjugate vaccine (2) Multiple platforms (3)

AMR Antimicrobial resistance RI Routine immunisation UPHN Unmet public health needs

	POPULATION	STATUS	PLATFORM
RESPIRATORY SYNCYTIAL VIRUS (RSV)[34, 35, 36] • RSV is a globally prevalent cause of lower respiratory tract infection in all age groups. • RSV accounts for hospitalisation of 1 in 5 young children < 5 years diagnosed with acute lower respiratory infections and 1 in 6 in adults > 65 years. • Annually, the virus is estimated to cause 33 million cases and 66,000 to 199,000 deaths of children below five years. **Vaccines in the pipeline: 6 (RSV) + 2 (influenza + RSV) + 1 (COVID-19 + influenza + RSV) + 1 (COVID-19 + RSV)**	Paediatric (3) Adults (1) Adults + older adults (2) Older adults (3) N/A (1)	Phase I (5) Phase II (2) Phase III (2) Under review (1)	Live-attenuated virus (1) mRNA (6) Protein nanoparticles (1) Protein subunit (1) N/A (1)
MEASLES, MUMPS, RUBELLA, VARICELLA[37, 38, 39, 40] • Acute, highly contagious disease caused by varicella-zoster virus (VZV). Following infection, most often in early childhood, the virus remains latent in neural ganglia and can be reactivated later in life to cause herpes zoster, or shingles. Almost one-third of the population will experience an outbreak of shingles during their lifetime. • Varicella is more severe in adults than in children and can be fatal especially in neonates and in immunocompromised individuals. • In the USA, around 4 million annual varicella cases reported with 100–150 deaths and more than10,000 hospitalisations before the introduction of routine varicella vaccination. **Vaccines in the pipeline: 1**	Paediatric (1)	Phase II (1)	Live-attenuated virus (1)
VARICELLA-ZOSTER VIRUS (VZV)[41, 42, 43] • Varicella is an acute, highly contagious disease caused by varicella-zoster virus (VZV). Following infection, most often in early childhood, the virus remains latent in neural ganglia and can be reactivated later in life to cause shingles. Almost one-third of the population will experience an outbreak of shingles during their lifetime. • Varicella is more severe in adults than in children and can be fatal especially in neonates and in immunocompromised individuals. • In the US, around 4 million annual varicella cases reported with 100-150 deaths and more than 10,000 hospitalisations before the introduction of routine varicella vaccination. **Vaccines in the pipeline: 2 (varicella) + 1 (shingles)**	Paediatric + adults + older adults (1) Adults + older adults (1) N/A (1)	Phase I (1) Phase II (2)	Live-attenuated virus (1) mRNA (2)

*4 vaccine candidates against meningococcal A, B, C, W, Y disease, 2 vaccine candidates against meningococcal A, C, W, Y disease and 1 vaccine candidate against meningococcal B disease.

TRAVEL VACCINES

In the 21st century, more people are travelling and migrating than ever before, increasing the risk of spreading infectious diseases. It is estimated that between 42% and 79% of travellers to low- and middle-income countries become ill with a travel-associated disease. While most of these health issues are mild, there are a significant number of cases when the help of a healthcare professional is requested.[44] An analysis evaluating the travel-related infections present in Europe over a 20-year period revealed that the most frequently diagnosed diseases are influenza and malaria, with infections caused by arboviruses being on an upward trend (e.g., dengue, chikungunya, Zika, yellow fever, West Nile fever).[45]

Travel vaccines are those recommended to protect people travelling to and from areas with endemics of severe diseases not found other parts of the world, and they differ depending on the area of travel. Vaccination is pivotal in protecting international travellers and preventing the importation of vaccine-preventable diseases, including, but not limited to, cholera, chikungunya virus, dengue fever, hepatitis A, B, and E, Japanese encephalitis, malaria, meningococcal disease, polio, rabies, tick-borne encephalitis, typhoid fever, and yellow fever.[46,47]

Travel vaccine candidates against chikungunya virus, dengue fever, malaria, meningococcal disease, rabies, typhoid fever and yellow fever are currently in development in the pipelines of Vaccines Europe members.

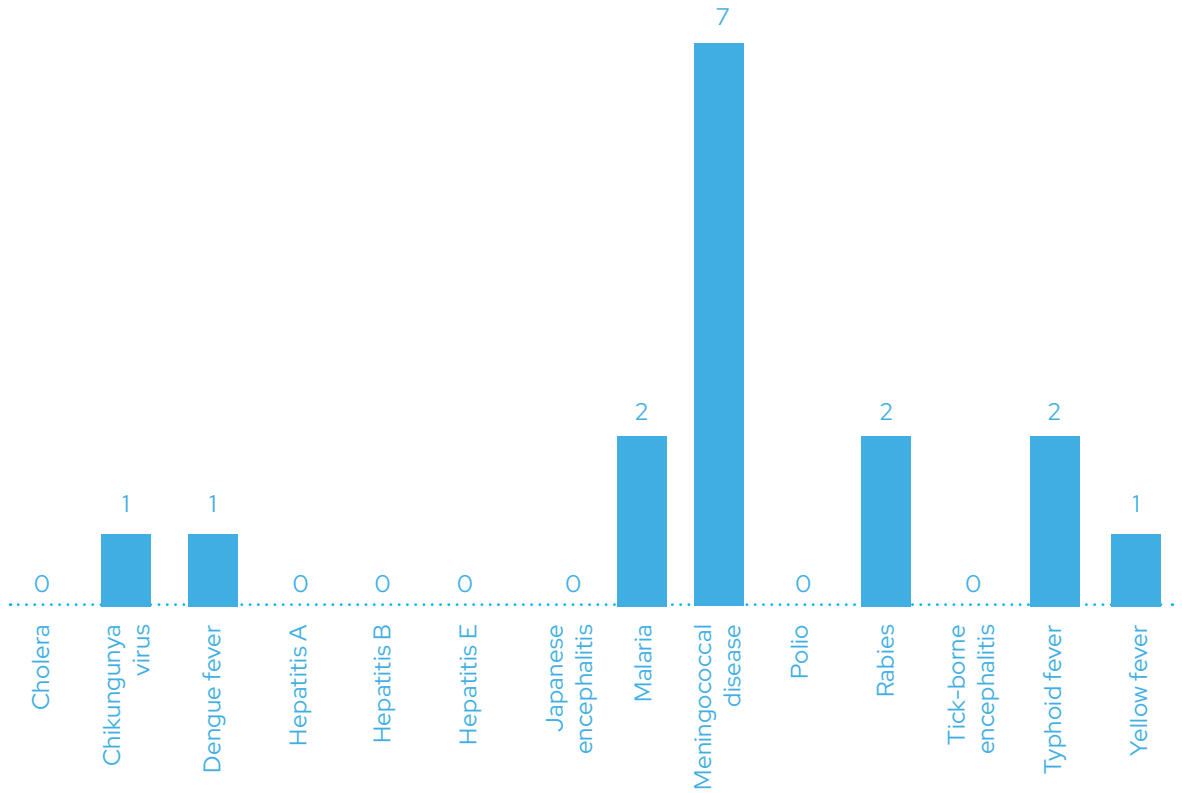


Figure 9. Number of travel vaccines in the pipeline.

*There are two vaccine candidates against hepatitis B in the pipeline, however they are intended for therapeutic use and therefore have not been included in this figure.

AMR Antimicrobial resistance
CC Climate change
RI Routine immunisation
TrV Travel vaccines
UPHN Unmet public health needs
ZOO Zoonoses

	POPULATION	STATUS	PLATFORM
CHIKUNGUNYA VIRUS[48, 49, 50] • Viral disease caused by the chikungunya virus transmitted to humans by infected mosquitoes. • Over 300,000 reported cases in the first half of 2023 and more than 300 deaths worldwide. • Over 106,000 disability-adjusted life years (DALYs) lost on average annually from 2010 to 2019 due to chikungunya infection. • Currently no vaccine or specific drug against the virus. **Vaccines in the pipeline: 1**	Adults (1)	Phase III (1)	Live-attenuated virus (1)
DENGUE FEVER[51, 52, 53] • Mosquito-borne viral disease affecting humans worldwide. • Half of the world's population now at risk of dengue with an estimated 100–400 million infections occurring each year. • Approximately 20,000-25,000 deaths mainly in children. **Vaccines in the pipeline: 1**	Paediatric + adults + older adults (1)	Phase II (1)	Live-attenuated virus (1)
YELLOW FEVER[54, 55] • Acute viral haemorrhagic disease transmitted by infected mosquitoes. • 200,000 cases and 30,000 deaths each year, with 90% occurring in Africa. • 20% to 50% of infected persons who develop severe disease die. **Vaccines in the pipeline: 1**	Paediatric + adults + older adults (1)	Phase II (1)	Live-attenuated virus (1)

ANTIMICROBIAL RESISTANCE

Drug-resistant infections are already common, resulting in longer hospital stays and higher medical costs, as well as increased mortality. In 2019, 4.91 million deaths were associated with bacterial AMR and the number could rise to 10 million deaths per year globally by 2050, generating costs from $300 billion to more than $1 trillion annually by 2050.[3,4] Across the EU/EEA region and the UK, the health burden of infections due to AMR is comparable to that of influenza, tuberculosis and HIV/AIDS combined and it is estimated that by 2050, AMR will result in over 569 million extra hospital days annually.[56]

Vaccination has been widely recognised as an indispensable tool in the fight against AMR.[57, 58, 59, 60, 61] Vaccines are effective before bacteria start to multiply and before different tissues and organs are affected. This decreases the likelihood of resistant mutations spreading. Available evidence demonstrates that the introduction of the pneumococcal conjugate vaccine in the US has resulted in an 84% reduction in an invasive disease caused by drug-resistant *Streptococcus pneumoniae* in children under two years of age.[62] Positive outcomes were also observed with vaccination against *Haemophilus influenzae* type b (Hib).[63] A recent study examined the vaccine-avertable AMR burden in a baseline scenario for vaccination of primary age groups against 15 pathogens. It found that vaccines could help to avoid 0.51 million deaths and 28 million disability-adjusted life-years (DALYs) associated with bacterial AMR, and 0.15 million deaths and 7.6 million DALYs attributable to AMR globally in 2019.[64]

Developing vaccines that address resistant pathogens is an extremely challenging task. However, Vaccines Europe members are playing their part in addressing AMR, in line with the strategy developed by the WHO as a technical annex to the Immunisation Agenda 2030.[65]

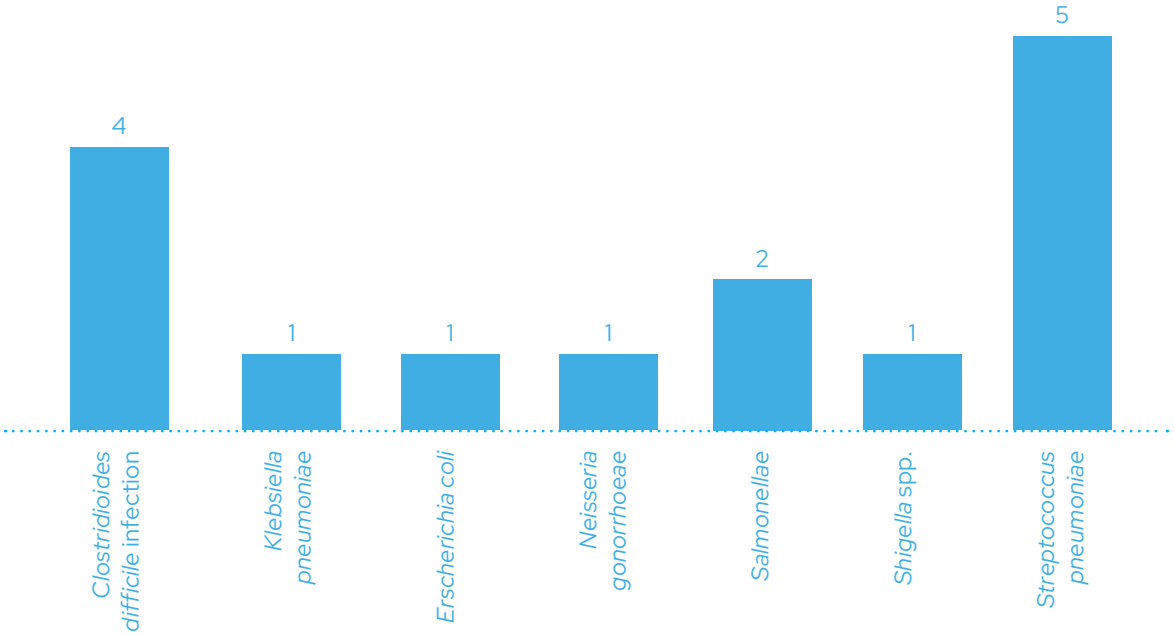


Figure 10. Number of vaccine candidates addressing antibiotic-resistant microorganisms.

Vaccines that prevent viral infections also play an important role in decreasing the overuse and misuse of antibiotics, either by reducing erroneous prescriptions that encourage the inappropriate treatment of viral diseases with antibiotics, or by preventing secondary bacterial superinfections.[66] There is increasing evidence in this direction for vaccination against rotavirus, influenza, varicella and dengue[67, 68, 69, 70] and similar trends are expected for COVID-19 and RSV. For example, a recent study showed that administering an RSV vaccine to pregnant mothers would reduce antimicrobial prescribing for their infants by 12.9% over the first three months of life.[71] When it comes to COVID-19, evidence shows that between 2020 and 2022, antibiotics were prescribed to approximately 75% of patients with COVID-19, even if fewer than 10% of them developed bacterial co-infection.[72]

There are currently 15 vaccine candidates in our members' pipelines that are targeting antibiotic-resistant bacteria on the WHO's priority pathogens list.[73] Additionally, their pipelines contain 50 candidates against COVID-19, dengue, influenza, RSV and varicella/shingles.

AMR Antimicrobial resistance RI Routine immunisation UPHN Unmet public health needs

	POPULATION	STATUS	PLATFORM
CLOSTRIDIOIDES DIFFICILE [74, 75] AMR, RI, UPHN • Nearly 124,000 healthcare-associated *C. difficile* infections (CDIs) annually in acute care hospitals in the EU/EEA, and 3,700 deaths. • 1 in 11 people over age 65 diagnosed with a healthcare-associated CDI dies within one month. • Currently no licensed vaccine for the prevention of CDI. **Vaccines in the pipelines: 4**	Adults + older adults (2) Older adults (1) N/A (1)	Phase I (2) Phase II (1) Phase III (1)	Protein subunit (2) Toxoid vaccine (2)
INVASIVE *ESCHERICHIA COLI* DISEASE [76, 77, 78, 79] AMR, UPHN • Leading cause of adult sepsis and bacteraemia and the second most common cause of neonatal meningitis. • Great impact on public health and economic burden due to high incidence of infections and antimicrobial resistance. **Vaccines in the pipeline: 1**	Older adults (1)	Phase III (1)	Glycoconjugate vaccine (1)
KLEBSIELLA PNEUMONIAE [80, 81, 82] AMR, RI, UPHN • Bacteria that can cause community-acquired and hospital-acquired infections (pneumonia, bloodstream infections, wound or surgical site infections, and meningitis). • *K. pneumoniae* accounts for approximately 11.8% of all hospital-acquired pneumonia in the world. • Percentage of *Klebsiella pneumoniae* resistant to a type of antibiotics called carbapenems slowly increased from 8% in 2014 to 10% in 2020. **Vaccine in the pipelines: 1**	Adults + Older adults (1)	Phase I (1)	Glycoconjugate vaccine (1)

AMR Antimicrobial resistance RI Routine immunisation UPHN Unmet public health needs

	POPULATION	STATUS	PLATFORM
GONORRHOEA[83] • Preventable and curable sexually transmitted infection caused by the bacterium *Neisseria gonorrhoeae*. • In 2020 there were an estimated 82.4 million new infections among adults globally. • Increasing antimicrobial resistance to antibiotics has been observed in *N. gonorrhoeae*. **Vaccines in the pipeline: 1**	Paediatric + adults (1)	Phase II (1)	Generalised modules for membrane antigens (1)
SHIGELLOSIS[84, 85] • Gastrointestinal infection caused by one of four species of *Shigella*. • 450,000 infections in the US each year and an estimated $93 million in direct medical costs. Of these, 77,000 infections are antibiotic resistant. • Over 8,400 confirmed shigellosis cases in 2019 in the EU/EEA. **Vaccine in the pipelines: 1**	Adults (1)	Phase II (1)	Generalised modules for membrane antigens (1)
STREPTOCOCCUS PNEUMONIAE[86, 87] • *Streptococcus pneumoniae (S. pneumoniae)* is the leading cause of community-acquired pneumonia. • Incidence of community-acquired pneumonia caused by *S. pneumoniae* is 1 in 1,000 adults per year. • 1 million children die of pneumococcal disease every year. • Pneumococcal resistance to antimicrobials is a serious and rapidly increasing problem worldwide. **Vaccines in the pipelines: 5**	Paediatric (2) Adults (2) Paediatric + adults + older adults (1)	Phase II (2) Phase III (3)	Antigen-presenting cells (2) Glycoconjugate vaccine (3)

INFECTION-RELATED THERAPEUTIC VACCINES

Therapeutic vaccination is a field still in its infancy compared to preventive vaccines. There is no established regulatory and access environment pathway for therapeutic vaccines. They work by utilising a patient's own immune system to fight/control an existing infection or infection-related disease, rather than immunising for prevention of a future disease. Therefore, the aim of therapeutic vaccination is to boost or redirect the immune response and help to control or clear the disease caused by an infection.

CR Infection-associated cancer vaccines ThV Therapeutic vaccines UPHN Unmet public health needs

	POPULATION	STATUS	PLATFORM
HEPATITIS B[88] • Viral infection that attacks the liver and can cause both acute and chronic disease. • 296 million people living with chronic hepatitis B infection in 2019, with 1.5 million new infections each year. • Estimated 820,000 deaths in 2019, mostly from cirrhosis and hepatocellular carcinoma (primary liver cancer). **Vaccines in the pipeline: 2***	Adults (2)	Phase II (2)	Multiple platforms (1) Virus-like particle (1)
HERPES SIMPLEX VIRUS (HSV)[89, 90] • 2 types of HSV: HSV-1 and HSV-2. They can cause oral herpes (HSV-1), genital herpes (HSV-1 and HSV-2) and eye infection leading to blinding complications (HSV-1 and HSV-2). • 3.7 billion people under age 50 (67%) with HSV-1 infection globally. • 491 million people aged 15-49 (13%) worldwide with HSV-2 infection. • Like varicella zoster virus, latent HSV infection can re-activate and lead to recurrent outbreaks of symptoms. **Vaccines in the pipeline: 2***	Adults (2)	Phase I (1) Phase II (1)	Protein subunit (1) mRNA (1)

*Therapeutic vaccine

INFECTION-ASSOCIATED CANCER VACCINES

Two main approaches are considered:

- **prophylactic:** refers to the prevention of infection-related cancers, such as liver cancer that could be a consequence of hepatitis B infection, or those related to infection with HPV or the Epstein-Barr virus
- **curative:** induce tumour regression, eradicate minimal residual disease, establish lasting antitumour memory and avoid non-specific or adverse reactions[91]

This review only includes vaccines targeting infectious agents.

CR Infection-associated cancer vaccines
RI Routine immunisation
ThV Therapeutic vaccines
UPHN Unmet public health needs

	POPULATION	STATUS	PLATFORM

EPSTEIN-BARR VIRUS (EBV)[92, 93]

CR RI UPHN

- The first human tumour virus discovered, being strongly involved in the aetiology of multiple lymphoid and epithelial cancers.
- EBV is also the primary cause of infectious mononucleosis.
- Over 200,000 new EBV-associated cases of cancer and 150,000 deaths worldwide annually.
- Up to 70% of adolescents and young adults in developed countries suffer from infectious mononucleosis caused by EBV.
- Currently no vaccines or treatments against EBV infection.

Vaccines in the pipeline: 2

POPULATION	STATUS	PLATFORM
Adults (2)	Phase I (2)	mRNA (2)

GLIOBLASTOMA (CMV-MEDIATED)[94, 95]

CR ThV

- Fast-growing and aggressive brain tumour that can result in death in six months or less, if untreated.
- Incidence of 3.21 per 100,000 population.
- GBM presents unique treatment challenges due to the localisation of tumours in the brain.
- Approximately 40% survival in the first year post-diagnosis and 17% in the second year.
- Cytomegalovirus (CMV) plays a crucial role in the pathogenesis and treatment of glioblastoma, but among glioma patients with confirmed CMV infection, a low pathological positive rate was associated with better prognosis and longer survival.

Vaccines in the pipeline: 1

POPULATION	STATUS	PLATFORM
Adults + older adults (1)	Phase II (1)	Virus-like particle (1)

HUMAN PAPILLOMAVIRUS (HPV)[96, 97]

CR RI

- Group of viruses that can cause cervical cancer, which is the second most common type of cancer in women aged 15–44 years.
- Each year, there are around 33,000 cases of cervical cancer in the EU, and 15,000 deaths.
- At global level, there were approximately 604, 000 new cases and 342,000 deaths in 2020. About 90% of the new cases and deaths in 2020 occurred in low- and middle-income countries.

Vaccines in the pipeline: 1

POPULATION	STATUS	PLATFORM
Paediatric + adults (1)	Phase II (1)	Protein subunit (1)

Addressing global health threats

CLIMATE CHANGE

Climate change is having a serious effect on global health. Approximately 58% of infectious diseases are believed to be aggravated by global warming and extreme weather due to increased spread of disease vectors like mosquitoes and changes in the lifecycles of pathogens.[98]

Vector-borne diseases

Warming temperatures and increased rainfall can result in mosquitoes expanding beyond their existing geographical range, leading to an increased risk of diseases like West Nile fever, Zika, dengue fever, chikungunya, malaria and yellow fever. These diseases cause more than 700,000 deaths each year, accounting for over 17% of all infectious diseases.[99]

Projections indicate a rise in the environmental conditions suitable for *Aedes albopictus*, the vector carrying dengue, chikungunya and Zika virus. Additionally, there has been an increase in the annual length of season suitable for malaria transmission across Europe since 1950. These estimates highlight an increased likelihood of local transmission of these diseases.[100]

Water-borne diseases

It is estimated that more than 3.4 million people die annually due to water-borne and sanitation-related diseases, such as cholera, rotavirus, typhoid fever (*Salmonella sp.*) and dysentery (*Shigella sp., E. coli*). The contamination of water supplies with these pathogens is expected to increase as a consequence of climate change, due to high temperatures, flooding, droughts and storms.[99]

Food-borne diseases

Every year, approximately 600 million people become sick worldwide due to contaminated food. Heavy rains, flooding and high temperatures increase the spread of pathogens into watersheds and croplands and will accelerate their replication cycles, increasing the risk of food contamination with pathogens such as *Salmonella* and *Campylobacter*.[99]

Additionally, disruption to the habitats of bats, rodents, and primates can drive these animals to areas where humans are living, making zoonotic exposures more likely. Melting ice and thawing permafrost can expose ancient deadly pathogens, such as anthrax.

Climate change can also impact human behaviour. Extreme weather, such as heatwaves and heavy rainfall, can drive people to cluster together indoors more often, making it easier for infectious diseases to spread. In addition, as humans adapt to changes in temperature, our immune systems can be weakened, making us more vulnerable to respiratory diseases like influenza.

A report issued by the World Bank in 2021 describes how climate change could force 216 million people to migrate within their own countries by 2050,[101] due to the impact on their livelihoods and loss of liveability in highly exposed locations. It is vital that we prepare now for the cross-border health threats posed by climate change.

The pipelines of Vaccines Europe members include vaccine candidates against chikungunya virus, dengue fever, malaria, typhoidal and non-typhoidal *Salmonella*, *Shigella sp.*, yellow fever and Zika.

AMR Antimicrobial resistance | CC Climate change | RI Routine immunisation | TrV Travel vaccines | UPHN Unmet public health needs | ZOO Zoonoses

	POPULATION	STATUS	PLATFORM
MALARIA[102] • Life-threatening disease caused by *Plasmodium* parasites that are transmitted to people through the bites of infected female mosquitoes. • Left untreated, malaria can progress to severe illness and death within a period of 24 hours. • In 2021, 247 million cases of malaria worldwide and 619,000 deaths. • In 2021, 95% of malaria cases and 96% of malaria deaths occurred in the WHO African region. Children under five accounted for about 80% of all malaria deaths in the region. **Vaccines in the pipelines: 2**	Paediatric (1) Paediatric + adults (1)	Phase II (1) Phase III (1)	Protein subunit (1) Protein nanoparticles (1)

SALMONELLA[103, 104, 105]
• Categorised as typhoidal and non-typhoidal serotypes.
• Increasing resistance to various types of antibiotics.
• Typhoidal: cause typhoid and para-typhoid fever, resulting in approximately 9 million cases and 110,000 deaths every year.
• Non-typhoidal:
  • 1 of 4 key global causes of diarrhoeal diseases; most cases of salmonellosis are mild, but sometimes they can be life-threatening.
  • In Europe the second most common food-borne zoonosis in 2020, with 54,702 confirmed human cases.
Vaccines in the pipeline: 2 (1 for typhoidal and paratyphoidal *Salmonella*, 1 for typhoidal and non-typhoidal *Salmonella*)
	Adults (2)	Phase I (2)	Glycoconjugate vaccine (1)
			Generalised modules for membrane antigens (1)

ZIKA[106, 107, 108] • Disease caused by a virus transmitted primarily by infected mosquitoes. • Over 707,000 Zika virus disease cases reported in the Americas in 2015-2016. • Infection during pregnancy is associated with complications such as preterm birth and miscarriage or can cause infants to be born with microcephaly and other congenital malformations. • An increased risk of neurologic complications is associated with Zika virus infection in adults and children. • Currently no licensed vaccines or treatments for Zika. **Vaccine in the pipelines: 3**	Paediatric + adults (1) Adults (2)	Phase I (2) Phase II (1)	RNA (1) Whole-inactivated virus (2)

ZOONOSES AND PANDEMIC PREPAREDNESS

Zoonotic diseases are those transmitted from animals to humans. It is estimated that 60% of infectious diseases in humans can be attributed to animal origin. Many of these diseases have high mortality rates and the potential to cause epidemics and pandemics. Zoonotic diseases are responsible for approximately 2.7 million deaths and 2.5 billion human illnesses annually, in addition to impacting livestock production and food security.[109]

COVID-19 is believed to have originated in animals. Monkeypox, avian influenza, and several other viruses carrying zoonotic infection potential circulating in farmed and wild animals, are a constant reminder that another pandemic could be around the corner. While it is important to implement robust measures to predict and prepare for the outbreak of zoonotic infectious diseases, it is equally important to prevent their emergence.

Vaccines Europe members are addressing the challenge of zoonotic diseases by researching vaccines against chikungunya, coronaviruses, dengue fever, influenza, Lyme disease, malaria, rabies, Nipah virus disease, salmonellosis and yellow fever.

The COVID-19 pandemic has stressed the need to strengthen the One Health approach, which focuses on the interconnectivity between the health of human communities, animals, and the environment. This will require strong transdisciplinary collaboration across the sciences. A joint report issued by European Centre for Disease Prevention and Control (ECDC), European Food Safety Authority (EFSA), European Medicines Agency (EMA), and Organisation for Economic Co-operation and Development (OECD) in March 2022 emphasised that a One Health approach is essential for the future of animal and public health.[110]

AMR Antimicrobial resistance | RI Routine immunisation | TrV Travel vaccines | UPHN Unmet public health needs | ZOO Zoonoses

	POPULATION	STATUS	PLATFORM
CORONAVIRUSES INFECTIONS[111, 112, 113] • Most coronaviruses infect animals (i.e., birds and mammals - bats and pangolins), which act as reservoirs and intermediate hosts, but can sometimes change host and infect humans. • There are currently seven coronaviruses known to infect humans, four of them causing mild-to-moderate disease and three of them causing more severe and possibly even fatal disease (SARS- CoV, MERS-CoV, SARS-CoV-2). • MERS-CoV: from 2012 to May 2023, over 2,600 confirmed cases, with a death rate of 36%. • SARS-CoV2 (COVID-19): over 700 million confirmed cases, with over 6 million deaths. **Vaccines in the pipeline: 18 (coronaviruses) + 3 (influenza + SARS-CoV-2) + 1 (influenza + SARS-CoV-2 + RSV) + 1 (SARS-CoV-2 + RSV)**	Adults (5) Adults + older adults (11) Paediatric + adults + older adults (3) N/A (3)	Phase I (8) Phase II (7) Phase III (6) Under review (2)	Monoclonal antibody (2) Protein nanoparticles (3) mRNA (14) Virus-Like particle (3)
LYME DISEASE[114, 115] • Caused by the bacterium *Borrelia burgdorferi* and transmitted to humans by the bite of infected ticks. • Around 476,000 cases diagnosed and treated per year in the US, and over 200,000 cases per year in Western Europe. • If left untreated, infection can spread to joints, the heart, and the nervous system. • Currently no vaccine available. **Vaccines in the pipeline: 2**	Paediatric +adults (1) Adults (1)	Phase I (1) Phase III (1)	Protein subunit (1) mRNA (1)
NIPAH VIRUS INFECTION[116, 117] • Estimated fatality rate 40% to 75%. • 639 human cases of Nipah virus infection reported from Bangladesh, India, Singapore, Philippines and Malaysia, with a mortality rate of about 59% until 2018. • Fruit bats are the wildlife reservoir of Nipah virus. • Currently no treatment or vaccine available against Nipah virus. **Vaccines in the pipeline: 1**	Adults (1)	Phase I (1)	mRNA (1)
RABIES[118, 119] • Viral disease that causes tens of thousands of deaths every year, mainly in Asia and Africa. • Dogs are the main source of human rabies deaths, contributing up to 99% of all rabies transmissions to humans. • Estimated global cost of US$ 8.6 billion per year. **Vaccines in the pipeline: 2**	Adults (1) Paediatric + adults + older adults (1)	Phase I (1) Phase III (1)	mRNA (1) Whole-inactivated virus(1)

Platform technologies

Vaccine manufacturing has evolved over the years to overcome limitations and reflect technological advancements, with a wide variety of platform technologies being developed and perfected over time.

The pipeline review revealed that the technology used for most vaccine candidates is mRNA. However, all other technologies are well represented and equally important. Two relatively new technologies included in this year's pipeline review are GMMA vaccines (generalised modules for membrane antigens) and monoclonal antibodies for prophylactic use.

Diversification of vaccine technologies is key to addressing a range of diseases, allowing for tailored solutions to combat different pathogens. It also ensures patients are provided with a choice of vaccines to meet their needs, considering the diverse immune responses of the populations based on factors such as age, genetics and health status, as well as their individual preferences. Additionally, a wide portfolio of vaccines technologies supports better access to vaccination at global level, having in mind that infrastructures, resources and healthcare systems vary between regions. Finally, in case of a global health threat, such as a pandemic, having multiple platforms available can accelerate the development of vaccines and support faster protection of populations.

Combination vaccines are an approach that has been used for many years in routine immunisation, for example MMR (measles, mumps, rubella) and DTaP (diphtheria, tetanus, acellular pertussis). It is a valuable tool for reducing the number of injections needed to protect against multiple diseases and for better fitting the vaccination schedule. Several types of combination vaccines are currently under development, such as SARS-CoV-2 + influenza (+/- RSV), human metapneumovirus + RSV, and measles + mumps + rubella + varicella (MMRV).

Adjuvants are present in many of the vaccine candidates, their main aim being to enhance the body's immune response to vaccine antigens. A wide range of adjuvants are used by Vaccines Europe members in their candidate products, from well-known ones to innovative adjuvants developed by each company. Examples of adjuvants used in their pipelines are alum (aluminium salts, usually phosphate or hydroxide), AS01, AS03, E6020, MF58, Matrix-M and GM-CSF. The composition of these adjuvants varies and consists of different natural or synthetic substances, such as oils, lipids found on the outer membrane of bacteria, salts, surfactants, saponins, liposomes and proteins.

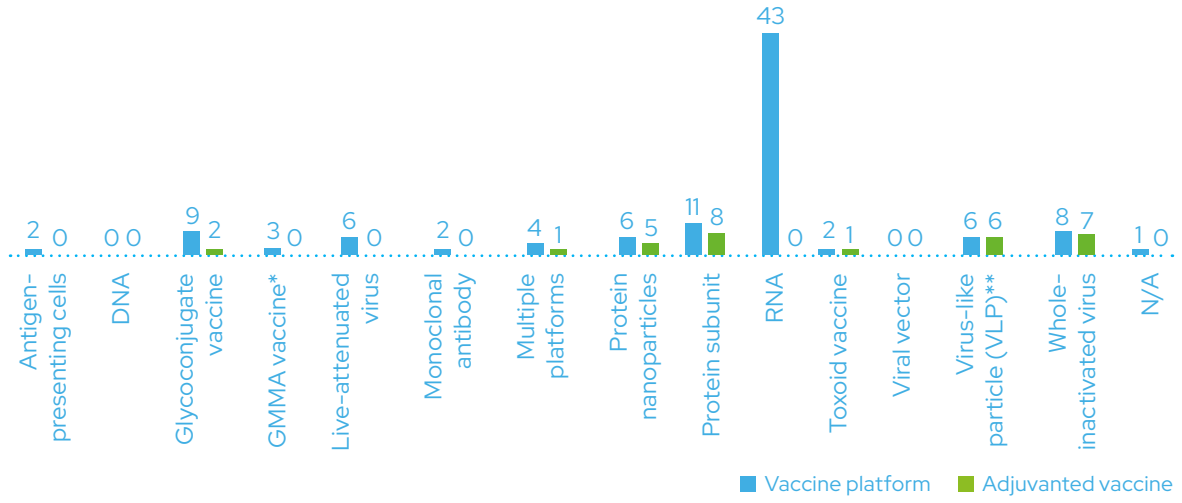


Figure 11. Number of vaccines in development by platform technology.

*Generalised modules for membrane antigens

**including enveloped VLP (eVLP)

Conclusion

During the COVID-19 pandemic, significant resources were dedicated to developing, manufacturing, distributing and administering vaccines against SARS-CoV-2. The virus is still present in communities, and vaccine manufacturers continue to work on bringing a wide variety of COVID-19 vaccines to the market to protect the populations across the globe. However, we also observe an increased focus on other research areas compared to last year and there has been progression of promising candidate vaccines to the next development stages. While the world was not well prepared for the COVID-19 pandemic, there are many known public health threats ahead of us for which we need to be ready.

In the interconnected world we live in today, vaccines support us to travel more safely in many areas across the globe. While vaccines against all these diseases are not yet on the market, the report highlights the ongoing work conducted by pharmaceutical companies to make travelling even safer for all of us.

Vaccines are proven to bring considerable value to individuals, but also to society, saving millions of lives every year. They improve the efficiency of healthcare systems, support socio-economic progress, and address the serious cross-border health threats of the future. To take full advantage of all the benefits they bring, it is important to adopt a life-course approach to vaccination. The pipelines of vaccine manufacturers show their commitment to develop vaccines for populations of all ages to ensure that everyone has the chance to be protected against vaccine-preventable diseases.

Vaccines are very complex biological products, and it takes many years and resources to develop efficient vaccines that can be administered to the populations.

The pipeline review is a testimony of the commitment of vaccine manufacturers to deliver a diverse portfolio of vaccines that address many challenges of today and tomorrow, such as health emergencies, zoonoses and arboviruses, antimicrobial resistance and socio-economic and demographic changes, as well as the dangers posed by climate change.

But getting a vaccine from the lab to the population is a collaborative effort. Everyone has a role to play in ensuring that vaccines reach the people who need them, including: those involved in academia, biotech, pharma and clinical development; the regulators who review and approve new vaccines; the National Immunisation Technical Advisory Groups and health technology assessment bodies that assess them; the governments that provide funding, infrastructure and campaigns to support immunisation programmes; and the healthcare providers who inform patients, answer questions and administer the vaccines.

Improving and maintaining attractiveness for vaccine manufacturers is critical for the UK to be a key player in the research, innovation and manufacturing of vaccines that address the health needs of the population. Recent initiatives including strategic partnerships with industry and the creation of the UK Health Security Agency Vaccine Development and Evaluation Centre all help to create a positive environment for innovation.

Timely and equitable population access to vaccination prevents illness and saves lives. To achieve this, barriers to the adoption of vaccines into national immunisation programmes must be proactively identified and addressed. The NHS should be encouraged and supported to implement strategies that improve uptake of vaccination in the most under-served communities so that no one is left behind.

We must prepare for tomorrow, today.

ANNEX I – Summary of vaccine candidates based on the stage of clinical development

DISEASE	NUMBER OF VACCINE CANDIDATES	TRIAL POPULATION		
		PAEDIATRIC	ADULTS	OLDER ADULTS
PHASE I CLINICAL TRIALS				
Clostridioides difficile infection	2		✔	✔
Coronaviruses	5		✔	✔
COVID-19 + influenza	1	N/A	N/A	N/A
COVID-19 + influenza + RSV	1		✔	✔
COVID-19 + RSV	1	N/A	N/A	N/A
Cytomegalovirus	2		✔	
Epstein-Barr virus infection	2		✔	
Herpes simplex virus	1		✔	
Human immunodeficiency virus (HIV)	2		✔	
Human metapneumovirus and RSV (hMPV/RSV)	1	✔		
Influenza	3		✔	✔
Influenza (pandemic)	1		✔	
Influenza + RSV	2		✔	✔
Klebsiella pneumoniae	1		✔	✔
Lyme disease	1		✔	
Nipah virus	1		✔	
Norovirus	1		✔	
Rabies	1		✔	
Respiratory syncytial virus	1	✔		
Salmonellae	2		✔	
Varicella	1	N/A	N/A	N/A
Zika	2	✔	✔	

DISEASE	NUMBER OF VACCINE CANDIDATES	TRIAL POPULATION		
		PAEDIATRIC	ADULTS	OLDER ADULTS
PHASE II CLINICAL TRIALS				
Clostridioides difficile infection	1			✔
COVID-19	5	✔	✔	✔
COVID-19 + influenza	2		✔	✔
Dengue virus	1	✔	✔	✔
Glioblastoma*	1		✔	✔
Gonorrhoea	1	✔	✔	
Group B streptococcus infection**	1		✔	
Hepatitis B*	2		✔	
Herpes simplex virus*	1		✔	
Human papilloma virus (HPV)	1	✔	✔	
Influenza	6	✔	✔	✔
Malaria	1	✔		
Measles, mumps, rubella, varicella	1	✔		
Meningococcal disease (B and A, B, C, W, Y)	3	✔	✔	✔
Pneumococcal disease	2	✔	✔	
Respiratory syncytial virus	2	✔		✔
Shigellosis	1		✔	
Shingles	1		✔	✔
Varicella	1	✔	✔	✔
Yellow fever	1	✔	✔	✔
Zika	1		✔	
PHASE III CLINICAL TRIALS				
Chikungunya virus	1		✔	
Clostridioides difficile infection	1		✔	✔
COVID-19	6	✔	✔	✔
Cytomegalovirus	1		✔	
Invasive *Escherichia coli* disease	1			✔
Influenza	4		✔	✔
Lyme disease	1	✔	✔	
Malaria	1	✔	✔	
Meningococcal disease (A, C, W, Y and A, B, C, W, Y)	3	✔	✔	
Pneumococcal disease	3	✔	✔	✔
Rabies	1	✔	✔	✔
Respiratory syncytial virus	2	✔		✔
UNDER REVIEW BY A REGULATORY AUTHORITY				
COVID-19	2	✔	✔	✔
Influenza	3	✔	✔	✔
Meningococcal disease (A, C, W, Y)	1	✔		
Respiratory syncytial virus	1			✔

* Therapeutic vaccine
** Vaccine dedicated to maternal immunisation

ANNEX II – Development of the pipelines of Vaccines Europe members companies between 2022 and 2023

DISEASE	NUMBER OF VACCINE CANDIDATES IN 2022	MARKETING AUTHORISATION GRANTED**	DEVELOPMENT PROGRAMS DISCONTINUED	NUMBER OF VACCINE CANDIDATES IN 2023 (INCLUDING THE NEW CANDIDATES)
VIRAL INFECTIONS				
Chikungunya virus	2	0	1	1
COVID-19 (different strains)	27	9	3	17
COVID-19 + influenza	2	0	1	3
COVID-19 + RSV	0	0	0	1
COVID-19 + influenza + RSV	0	0	0	1
COVID-19 and/or other coronaviruses	1	0	0	1
Cytomegalovirus	4	0	1	3
Dengue fever	1	1	0	1
Ebola	2	1	1	0
Epstein-Barr virus infection (EBV)	1	0	0	2
Glioblastoma (via CMV)*	1	0	0	1
Hepatitis B*	2	0	0	2
Herpes simplex virus*	1	0	0	2
Human immunodeficiency virus (HIV)	3	0	1	2
Human papilloma virus (HPV)	0	0	0	1
Human metapneumovirus and parainfluenza virus 3 (hMPV/PIV3)	1	0	1	0
Human metapneumovirus and RSV (hMPV/RSV)	0	0	0	1
Influenza	9	0	0	16
Influenza (pandemic)	0	0	0	1
Influenza + RSV	0	0	0	2
Measles, mumps, rubella, varicella	0	0	0	1
Nipah virus	1	0	0	1
Norovirus	0	0	0	1
Rabies	2	0	0	2
Respiratory syncytial virus	10	2	4	6
Varicella/shingles	1	0	0	3
Yellow fever	1	0	0	1
Zika	3	0	0	3

* Therapeutic vaccine

** Marketing authorisation granted in at least one market globally, which may or may not include the UK

DISEASE	NUMBER OF VACCINE CANDIDATES IN 2022	MARKETING AUTHORISATION GRANTED	DEVELOPMENT PROGRAMS DISCONTINUED	NUMBER OF VACCINE CANDIDATES IN 2023 (INCLUDING THE NEW CANDIDATES)
BACTERIAL INFECTIONS				
Clostridioides difficile infection	3	0	0	4
Gonorrhoea	0	0	0	1
Invasive *Escherichia coli* disease	1	0	0	1
Group B streptococcus infection**	1	0	0	1
Klebsiella pneumoniae	1	0	0	1
Lyme disease	1	0	0	2
Meningococcal disease	6	0	0	7
Pneumococcal disease	4	0	1	5
Salmonella spp.	0	0	0	2
Shigellosis	1	0	1	1
Skin and soft-tissue Infections caused by *S. aureus*	1	0	1	0
PROTOZOAL INFECTIONS				
Malaria	2	0	0	2

** Vaccine dedicated to maternal immunisation

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Rue du Trône 108
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1050 Brussels - BELGIUM

www.vaccineseurope.eu

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Hay's Galleria, 2 Hay's Lane
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