Vaccines:
a life-saving choice

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Key Points

- Vaccination has saved more lives than any other medical intervention.
- Vaccines prevent infectious diseases that cause serious illnesses and deaths, especially in infants and the elderly.
- Vaccines against acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can prevent coronavirus disease 2019 (COVID-19).
- Vaccines can also prevent virus-induced cancer, such as cervical and liver cancer, caused by human papilloma virus (HPV) and hepatitis B virus, respectively.
- Vaccines are safe and continuously vigorously monitored, and the clinical benefits outweigh the risks.
- Vaccines are most effective in controlling the spread of infection in the community when the uptake of the vaccine is high in the whole population.
- Adverse publicity and unsubstantiated claims around vaccine side-effects perpetuated by anti-vaccine movements have resulted in a decline in uptake of certain vaccines in Ireland.
- A failure to vaccinate puts the health and lives of individuals at risk and results in resurgence of vaccine-preventable diseases in the community, as seen with recent outbreaks of measles and mumps in Ireland and other countries.

Executive Summary

Vaccination provides long-term protection against infectious diseases. It has prevented hundreds of millions of deaths from infectious diseases around the world, protecting against smallpox, polio, diphtheria and a wide range of childhood illnesses such as measles, mumps and whooping cough. Vaccination against SARS Coronavirus-2 is the means by which the COVID-19 pandemic will be brought under control.

First introduced more than 200 years ago, **vaccines are one of the safest medical interventions available and save more lives every year than antibiotics or surgery.**[1] We now have vaccines that can prevent certain cancers, and more are being developed all the time. Yet the powerful protection that vaccination can offer is now in danger. It is slowly being undermined by the incorrect view that vaccination is not safe.

Some parents of young children are withholding or delaying vaccination, a decision usually influenced by wrong information leading to the mistaken view that vaccination can be harmful. This misguided view is being driven at least in part by parents picking up faulty 'facts' from social media and accepting claims by bloggers that are not backed up by scientific evidence. Some are still listening to false claims on social media that the measles, mumps and rubella (MMR) vaccine can cause autism. This allegation was first made by a medical researcher over 20 years ago,[2] but was soon found to be completely wrong[3] and based on falsified medical data. This researcher was later stripped of his medical registration. Social media sites make claims that vaccination can trigger other conditions such as asthma or diabetes; this is not true. Unfortunately, some individuals accept medical information from unqualified, untrained sources rather than from their family doctor.

Failing to vaccinate puts a child at risk of contracting measles, whooping cough and other childhood illnesses. These diseases can be very serious and even **fatal** in infants and young children if they are not protected by vaccination. The decision not to vaccinate also poses a threat to the general community. If many people are vaccinated, then there are fewer people left in the community who can spread the infection to others.[4] If vaccination rates fall, however, it is much easier for measles or mumps to spread. Low vaccination rates today have triggered several measles outbreaks in Ireland and other countries. These outbreaks have caused fatalities in Ireland and can be prevented if the great majority of people are vaccinated.

Few young parents in Ireland today have ever feared infection by smallpox, polio or diphtheria, once common illnesses that caused many deaths. Smallpox was eradicated in 1980 by vaccination and similarly polio is on the brink of eradication. Diphtheria is now held in check by vaccination. But as the recent measles and mumps outbreaks have shown, common but serious diseases will come back if we

do not vaccinate. This is what makes it so concerning that some parents are withholding vaccination from their children despite the potential dangers of infection, either locally or from travelling to a place where a virus is still endemic.

All medical procedures carry some level of risk and childhood injections are no exception. The fact that vaccination involves the administration of medicines to otherwise healthy individuals presents an ethical dilemma. However, before their routine use in humans, all vaccines must be shown to be safe and effective in a high proportion of vaccinated individuals in clinical trials. There is stringent safety testing before regulatory approval and after the roll-out of large vaccination programmes the new vaccines are constantly monitored for rare side effects by Irish and international agencies, including Ireland's Health Products Regulatory Authority (HPRA), the European Medicines Agency (EMA), the US Food and Drug Administration (FDA) and the World Health Organisation (WHO). **The risk posed by not vaccinating is far greater than any risk associated with receiving a vaccine**. The health benefits of vaccination are evident from the dramatic reduction in the incidence of many infectious diseases in the pre-vaccine era compared with today.[5] (Table 1)

A new generation of vaccines has also emerged that can help prevent future cancers. The HPV (human papilloma virus) vaccine targets the virus that in later life can trigger cervical cancer. Some parents refused this vaccination for their children because of concerns about safety, despite the fact that the vaccine has been shown to have no long-term side effects and reduces the risk of developing cervical precancers by 90%.[6] High vaccine uptake is needed to reduce HPV infection and new cases of cervical cancer.

This expert statement from the Royal Irish Academy is published to provide clear and useful information about vaccination and the health benefits it provides, especially in a time when vaccines and vaccination policies have come into public debate and interest due to the COVID -19 pandemic.

History of vaccine development

Vaccination ranks as the most successful medical treatment yet introduced for the prevention of common human diseases.[7] Widespread vaccination made it possible to eradicate smallpox completely and eliminated polio from most countries in the world,[8] two major killers now happily a thing of the past in Ireland (Figure 1). The latest advances in molecular biology, microbiology and immunology are being used to develop new infectious disease vaccines all the time and now vaccines that prevent cancers are coming on stream. The first vaccine developed to prevent widespread deaths from smallpox was proven to be effective just over 200 years ago in scientific experiments by the English physician Edward Jenner. It was known that milk maids tended not to develop smallpox during outbreaks. He realised that those who had developed a minor infection from cowpox, a similar disease in cattle, somehow escaped smallpox infection and inferred that infection by cowpox blocked the

much more serious smallpox infection. Although the mechanism – immune system memory – was certainly not understood at the time, this did not stop Jenner developing the first true vaccine in 1798.

Once the vaccine was shown to work it went into widespread use and sharply reduced the smallpox death rate from a peak of one in five who contracted the disease. Clinics sprang up and people agreed to be inoculated in high numbers, and the method spread out around the world. There were doubters – just as there are today – who in the later 1800s rioted against compulsory vaccination, claiming it did not protect against smallpox, but the success of inoculation could not be denied. The smallpox vaccine was the tool that eliminated smallpox disease, which had raged and ravaged the world for centuries. By systematically vaccinating all the people in contact or nearby to each person with smallpox, we humans, together in an enormous effort led by the WHO, have made a disease extinct.[9] There has not been a single person with smallpox disease since one case in Somalia in 1977[10] and a laboratory-associated case in Birmingham in 1978.[11]

A number of vaccines for diseases in domestic animals were developed over the next few decades and there were efforts to develop additional human vaccines. This was successfully done in 1885 when Louis Pasteur and Émile Roux developed the first vaccine against rabies.[12] The development of new vaccines raced ahead with vaccines for two major killers typhoid and cholera introduced in the 1890s. Many more vaccines emerged during the twentieth century against TB, yellow fever, whooping cough, diphtheria, tetanus and polio amongst others. Vaccines will remain an important weapon in the battle against human disease and new types of safe, more potent vaccines will emerge. We will need them in the coming era when antibiotic resistance may place even greater demands on our armoury of treatment options.

What are vaccines?

Vaccines are weakened or killed bacteria or viruses, a purified component from a pathogen, genetic material (RNA or DNA) or vector viruses that contain the genetic material that will lead to the synthesis of selected components of pathogens which, when administered to a person, stimulate immune responses against the pathogen but are incapable of causing disease.

How vaccines are made: Traditionally vaccines were made from killed or weakened versions of microbes. For example, the current poliovirus vaccine is made from inactivated whole poliovirus, whereas the MMR vaccine is made from attenuated or weakened versions of measles, mumps and rubella viruses. Vaccines can also be made from components of microbes, called antigens, the parts of the microbe to which our immune system responds. These vaccines are more refined and tend to have fewer side effects, but need to be administered with other components, called adjuvants, which help to boost the immune response to the antigen. Examples include the vaccines against diphtheria, tetanus, whooping cough and meningitis.

Pathogens: Disease-causing bacteria, viruses, fungi or parasites.

Microbes: Microorganisms which often exist as single cells, although they can be multicellular, and include bacteria, viruses, fungi and parasites.

Vaccines – the success story of modern medicine

Prior to the development and introduction of the vaccines we have in use today, infectious diseases, such as polio, diphtheria and whooping cough were commonplace and resulted in severe morbidity in millions of infected individuals and loss of countless lives worldwide (Table 1). The successful introduction of the smallpox vaccine, which has resulted in the elimination of the smallpox virus from the globe, paved the way for development of a range of vaccines that save millions of lives and prevent hospitalisation of infants, children and adults suffering from debilitating infectious diseases.

How do vaccines work?

Vaccines harness the immune system: The success of vaccination is based on the power of our immune system. This includes a number of highly specialised cell types, each with a different job to do. They come into play as required when we are infected by a bacterium or virus, and move quickly to eliminate the invaders within days. Most importantly, the immune system responds to and 'remembers' the invader and will attack immediately if it returns. Vaccines trigger immune system memory without the person having to contract the illness. The vaccine primes the immune system and it is then ready to come into play to resist the polio, measles or mumps virus if a person is exposed.

Population (also known as herd) Immunity: The immunisation rate with a vaccine (vaccine uptake) must reach a certain threshold, usually greater than 80-95% of the target population, for the vaccine to be effective in the whole population. Population immunity can provide protection for people who have not themselves developed immunity by eliminating the spread of the microbe within the population. Population immunity is particularly important in protecting the most vulnerable, especially infants who are too young to have been vaccinated, but also immunosuppressed individuals who cannot be vaccinated. However, if immunisation rates fall below a critical threshold, the whole population, especially the most vulnerable, is put at risk.

Polio vaccine: Poliomyelitis or polio is caused by the poliovirus that invades the gastro-intestinal tract and can spread to the central nervous system causing paralysis. In the 1950s, between 100 and 500 people developed polio in Ireland each year. The polio vaccine was introduced in 1957 and the last recorded case of polio in Ireland was in 1984.[13] Thanks to vaccination, poliovirus will probably be the next pathogen to be eliminated from the globe.

MMR vaccine: The MMR vaccine, introduced in Ireland in 1988, is a highly effective combination vaccine against three different viruses, measles, mumps and rubella. It has dramatically reduced the incidence of these diseases. There were more than 6,000 cases of measles annually in Ireland in the 1950s and this had fallen to two cases in 2015.[14] However, 81 cases of measles were reported in Ireland in 2018 and around 70% of these were in individuals who had not been vaccinated. Poor MMR vaccine uptake, largely due to adverse publicity from anti-vaccine lobby groups via social media, is resulting in a resurgence of measles and mumps and this is a major cause for concern in Ireland and other countries. Following a recent outbreak of measles, a New York county banned unvaccinated children from attending schools and

visiting public spaces for a month. Highlighting the urgency of this, the WHO revealed that in 2018 more than 80,000 people in 47 European countries contracted measles, leading to 72 deaths.

Vaccines against meningitis: Bacterial meningitis is a very serious disease. Without treatment virtually everybody dies, and even with the best treatment about one in ten who get it may die, and another one in ten will be left with brain damage. It is caused by bacteria that invade the blood stream and can then enter the spinal cord and brain. The bacteria cause inflammation in the protective lining (meninges) of the central nervous tissue, which can be fatal. Thirty years ago, hundreds of children in Ireland contracted bacterial meningitis. In 2000, before the vaccines were used in Ireland, there were 590 cases of bacterial meningitis leading to 30 deaths.[15] By 2016 there were only 145 cases causing 8 deaths because the vaccines prevented most of them.

Vaccines against cervical and liver cancer: Cancer is a devastating condition and kills over 9,000 people annually in Ireland.[16] Treating cancer is difficult; chemotherapy, radiation and surgery cause many unpleasant side-effects and are not always effective. Cancer prevention is preferable to treatment and this is now becoming possible through vaccination. Two vaccines that prevent cancers caused by viruses are now licensed in Ireland, a vaccine against the human papilloma virus (HPV), which prevents cervical cancer in women, oropharynx and anal cancers in sexually active men and women, and the hepatitis B virus vaccine, which prevents liver cancer. Virtually all cases of cervical cancer are caused by HPV. There are 300 new cervical cancer cases in Ireland each year and despite medical and surgical treatment, around 90 of these will die from the cancer.[17] Most HPV-associated cancers and deaths are preventable by immunisation of pre-teenagers with the HPV vaccine, which is 95% effective against the strains of HPV in the vaccine.[18] In Ireland, the HPV vaccine has been offered to all girls in first year in second level schools since 2010 and since September 2019 to boys to prevent head and neck, penile and anal cancers in their later years. We have seen in the media how young wonderful women with cervical cancer are speaking out for more vaccination to prevent it, and for better screening programmes to detect it earlier.

***Vaccines against COVID-19*:** In December 2019, the world became aware of the emergence of a new pathogen in China later identified as SARS-CoV-2. This led to the COVID-19 pandemic, which we currently are grappling with. Testing approaches for the virus or immune responses to it were developed at impressive speeds. Advances have been made in the treatment of severe COVID-19 disease that can develop following infection with SARS-CoV-2. However, anti-viral drugs have shown limited efficacy against severe COVID-19. Alternatively, treatment approaches involving passive immunisation with convalescent serum, or cocktails of monoclonal antibodies against the receptor binding region of the SARS-CoV-2 spike protein, are showing some success when given early in disease.

The development and population-wide administration of COVID-19 vaccines offers the best way out of the pandemic. Several COVID-19 vaccines were developed and approved for emergency use within

one year of identification of the new disease. This contrasts with traditional vaccines, which took years to develop. This unusual speed has given rise to scepticism and vaccine hesitancy by some, but can be explained by two main factors. First, several countries invested large amounts of money in vaccine development and at-risk purchase of promising vaccines with as yet unproven safety and efficacy. This allowed the various phases of vaccine development to be run concurrently rather than consecutively. Second, many COVID-19 vaccines used modifications of vaccine platforms that have been developed over the last decade. One such platform is based on messenger RNA (mRNA), which encodes spike protein of SARS-CoV-2 and produces this protein when incorporated into human cells (e.g., BioNTech/Pfizer and Moderna vaccines). This mRNA platform is the product of many years of research mainly focused on the development of cancer vaccines and now successfully applied to the development of highly successful vaccines against SARS-CoV-2. The second platform involves introduction of the gene for spike protein into the DNA of innocuous adenovirus vectors, which are disabled further by deleting genes that are essential for the growth of the virus, thereby preventing the virus from spreading from the injection site (e.g., the Oxford/AstraZeneca vaccine and the Johnson & Johnson vaccine). Again, the safety of these platforms has been evaluated in very large studies for vaccines for other diseases even before evaluation of their safety as a COVID-19 vaccine. More traditional approaches such as inactivated whole SARS-CoV-2 preparations (e.g., Sinopharm and Sinovac vaccines) as well as purified recombinant spike protein (e.g., Novavax vaccine) have also been used to develop COVID-19 vaccines. Data from phase 3 efficacy trials have shown that COVID-19 vaccines developed using each of these four platforms are highly effective at preventing COVID-19. There is some evidence that certain of these vaccines also prevent infection, with SARS-CoV-2.[19] They also appear to be effective in older individuals and are suitable for use in children. Work is also ongoing on the development of attenuated SARS-CoV-2 vaccines and vaccines against SARS-CoV-2 variants of concern.

Vaccines – benefit versus risk

Vaccines have made a greater contribution to human health than any other medical intervention.[20] It is estimated by the WHO that five lives are saved each minute as a result of worldwide vaccination programmes. Not only have they saved countless lives, but since vaccines are inexpensive compared with the cost of hospitalisation for life-threatening diseases, they save healthcare systems billions of euros annually. However, like all medicines, vaccines can have side effects, but any risk must be assessed against the benefits of preventing debilitating and potentially life-threatening infectious diseases, and this assessment is based on sound scientific evidence carefully evaluated pre- and post-licensure by regulatory agencies, including the FDA, EMA and HPRA.

How do we know if a new vaccine is safe? This is a very important question for every new medicine, including vaccines. For a new human vaccine to be licensed for use in humans, the manufacturer must

describe in detail the product, and exactly how it has been created from well-characterised ingredients. Human vaccines undergo stringent testing for efficacy and safety in clinical trials, the results of which are assessed by the FDA, EMA, and the HPRA in Ireland. These agencies review all results in detail and give permission for, or prevent, manufacture and sale of the vaccine. The primary objective of these agencies is to protect us, the public, from medicines that are dangerous or do not work effectively. Information about each medicine licensed in Ireland can be found at www.hpra.ie. Most side-effects to vaccines are rare and minor, the most common of which is injection site reactions (redness, swelling, pain) (Figure 2). However, a very small proportion of vaccines has been associated with more severe side effects. For example, a vaccine against whooping cough, the whole cell pertussis vaccine, was associated with fevers and rare cases of febrile convulsions. This vaccine, first developed in the 1940s, was based on inactivated whole bacteria, but it was replaced in Ireland[21] and other developed countries in the 1990s with a more refined pertussis vaccine based on purified components of the bacteria that eliminated these side effects.

Immunisation with a flu vaccine against a swine influenza virus was associated with a higher incidence of narcolepsy in immunised children/adolescents compared with the general population in Ireland[22] and other European countries during 2009 and 2010. This vaccine was designed to protect against a possible pandemic from a swine influenza virus which caused serious complications and deaths in previously healthy people. This vaccine was discontinued in 2010.

More often than not, the side-effects rather than the benefits of vaccines make the news headlines, and these have been exploited by the anti-vaccine lobby groups to spread negative sentiments around vaccines in general. In 1998 Dr Andrew Wakefield at the Royal Free Hospital in London claimed a link between the MMR vaccine and autism.[23] The results were later found to be false, and Wakefield was struck off by the UK General Medical Council for serious professional misconduct, but nevertheless continues to propagate his misinformation in the USA via film and social media. Multiple follow up studies including a very large study in Denmark concluded that there was no link between the MMR vaccine and autism.[24] However, unfortunately the MMR controversy did significant damage to public confidence in vaccines and led to the already referred to re-emergence of outbreaks of measles and mumps.

The enormous value of the HPV vaccine as an effective means to prevent cervical cancer in women and other HPV-related cancers in men has been detailed above. The vaccine has also been the subject of unsubstantiated claims by the anti-vaccine movement that it can cause chronic fatigue syndrome. However, there is no scientific or medical evidence to back up this assertion. This has been very closely and rigorously examined by regulatory agencies such as the EMA in Europe. If an individual develops some medical syndrome after vaccination, this may be a coincidental phenomenon that can

also occur in people who have not been vaccinated. Proof of a causal relationship requires a comparison of the risks of developing the syndrome in the vaccinated versus unvaccinated populations.

HPV-related cancers kill around 100 women and 30 men in Ireland each year, cancers that are preventable by the highly effective HPV vaccine. However, like other vaccines against infections, it is only effective in the community as a whole if a significant proportion (>80–95%) of the target population is vaccinated. In Ireland, the uptake of the HPV vaccine dropped to around 50% in 2017, largely because of negative publicity perpetuated by the anti-vaccine movement. A number of campaigns started by vaccinated girls and women with cervical cancer, which provided clear consistent facts about the vaccine supported by health professions, led to the uptake of the vaccine to increase to 70% among adolescent girls. A recent study in *The Lancet Oncology* has suggested that in the absence of further intervention there will be 44 million new cases of cervical cancer worldwide in the next 50 years.[25] Global HPV vaccination and cervical screening could avert up to 12 million of these cases and could eventually eliminate all cases of HPV-induced cervical cancer. In Ireland, the HPV vaccination programme has been available for boys since 2019. The HPV vaccine can provide men with direct protection against HPV-related cancers and help reduce HPV spread among the population.

The future of vaccination: examples of vaccines in development

- A vaccine against *Staphylococcus aureus*, which is responsible for MRSA, a form of this bacteria which is resistant to many common antibiotics.
- A universal flu vaccine that will prevent infection with all strains of influenza virus, obviating the need for the annual flu vaccination.
- A more effective vaccine against tuberculosis (TB), which will treat or prevent TB in adults and children and tackle the problem of multidrug-resistant TB.
- A vaccine against malaria.
- New RNA vaccines against viruses such as hepatitis C or human respiratory syncytial virus, where traditional vaccine approaches have failed.
- The added advantage of the RNA platform is that vaccines can be readily modified to counteract newly emerging variant viruses.
- A vaccine that will prevent infection with different strains of HIV, which will tackle the AIDS pandemic and dispense with the need for expensive anti-viral drugs.
- Vaccines that will prevent or eliminate cancers by harnessing the immune system to directly kill tumour cells.
- Unconventional vaccines designed to exploit immune system control of diseases such as diabetes, multiple sclerosis, rheumatoid arthritis or Alzheimer's disease.

Vaccines will continue to prevent millions of deaths from infectious diseases each year, and with the aid of research discoveries on disease mechanisms, have the capacity to tackle an even wider range of human diseases in the future.

Table 1. Health benefits of vaccination in the USA

Disease	20th Century annual number of cases[26]	2017 reported cases*	% Decrease
Smallpox	29,005	0	100%
Polio (paralytic)	1,316	0	100%
Diphtheria	21,053	0	100%
Haemophilus influenzae	20,000	33	>99%
Measles	530,217	120	>99%
Rubella	47,745	7	>99%
Mumps	162,344	6,109	96%
Tetanus	580	33	94%
Pertussis (whooping cough)	200,752	18,975	91%

*Data for cases in the US from the Centre for Disease Control, Atlanta;[27] Vaccination has had a similar impact on the incidence of infectious diseases in Ireland.

Figure 1. Vaccine-preventable infectious diseases. From left to right: Smallpox, meningococcal gangrene, whooping cough, measles and mumps. Images from the Centre for Disease Control, Atlanta.

Figure 2. Vaccination: A small pain for a greater gain.

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