MSD
INVENTING FOR LIFE

THE VALUE OF PAEDIATRIC VACCINATION

Protecting current and future generations across Europe

Executive summary

Paediatric vaccination is one of the most effective measures of disease prevention, protecting children and adults against serious, preventable and sometimes life-threatening diseases. Europe has a rich history of vaccine discovery, development and manufacturing and through advances in scientific research, there have been significant strides in the control and, in some cases, eradication of infectious childhood diseases.

Despite this impressive track record, vaccination coverage rates (VCR) are declining across Europe, causing unprecedented levels of outbreaks of vaccine-preventable diseases across the continent. European Union (EU) Member States have recognised the need for concerted action to effectively address increasing vaccination hesitancy and associated disease outbreaks. However, despite the encouraging policy action adopted by the European institutions, progress across Europe has remained frustratingly slow.

Informed by comprehensive research and insights gained through interviews with multi-disciplinary stakeholders in the field, this report makes a series of recommendations that aim to complement EU action on vaccination coverage to ensure people across Europe benefit from optimal protection from vaccine-preventable diseases.

The recommendations set out in this report fall under four key categories:

1. Increasing access to vaccination across the European Region

The coordination of vaccine decision-making across European healthcare systems and adequate funding of the service infrastructure are important steps towards ensuring that everyone is able to benefit from comprehensive access to vaccination, no matter where in Europe they live.

2. Changing societal perceptions in a sustainable way

Misconceptions around the impact of vaccination (risk vs. benefit) are some of the key drivers of vaccine hesitancy. Supporting healthcare professionals and teachers in providing comprehensive information about vaccination will ensure adequate understanding about its importance from an early age and encourage cross-generational sharing of knowledge.

3. Accelerating the use of digital tools and technologies

Addressing barriers to the wider implementation of digital immunisation records will provide individuals with a better understanding of their vaccination status and healthcare systems with comprehensive information about national coverage rates.

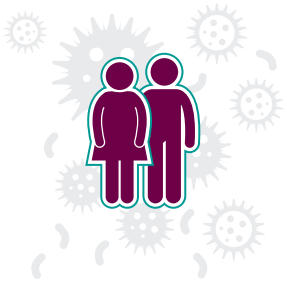
4. Elevating the level of innovation across the vaccination ecosystem

Ensuring that innovation in vaccination is adequately valued and incentivised will help healthcare systems across Europe harness the progress achieved in vaccination to date and encourage future research.

Introduction

Vaccination is one of the most powerful and cost-effective tools in the history of public health.[1] It is the most efficient method to prevent infectious diseases, saving millions of people from illness, disability and death each year.[2]

Paediatric vaccination has made a substantial contribution to reducing mortality globally. Today, nine out of 10 children in the WHO European region receive at least a basic set of vaccinations during infancy.[3] Over the past 40 years, widespread vaccination in Europe has eradicated smallpox[4] and polio.[5] Diphtheria and tetanus occur only rarely, and pertussis and rubella are better contained.[4]



The number of diseases that can be prevented by vaccination continues to grow. Today, individuals in Europe can be protected against up to 18 infectious diseases* through routine vaccination across their life-span.[6] Europe has a rich history of vaccine discovery, development and manufacturing. As a result of advances in scientific research, significant strides have been made in the control, elimination and, in some cases, eradication of infectious childhood diseases. Innovative vaccines provide protection against an increasing number of vaccine-preventable diseases, which include the prevention of cancer. Some innovative vaccines also help to simplify immunisation programmes (e.g. combination vaccines).[7]

Paediatric vaccination is a fundamental element of the life-course approach to vaccination, which underlines the importance of vaccination during all ages and stages of life.[8] In Europe, life expectancy is increasing while birth-rates are decreasing, resulting in an ageing population. Older adults must be prevented from getting ill to reduce the socio-economic burden on healthcare systems.[9] At the same time, we cannot afford to damage or even lose healthy young lives, as national wealth relies on the productivity and ability of the young generations.[10] This makes protecting individuals across the life-span crucial.

> It is unacceptable that in the 21st century our children still succumb to diseases that should not have existed in Europe for a long time
>
> Jean-Claude Juncker
> former President of the European Commission at the Global Vaccination Summit (2019)

Additionally, vaccination has been recognised as a key resource in the fight against antimicrobial resistance (AMR).[11] By reducing disease incidence, paediatric vaccination contributes to reducing the need for and potential misuse of antibiotics.[12] Vaccination also plays a key role in health protection in an era of evolving population dynamics due to global travelling and migration, and emerging crises of new diseases such as Ebola.[13] This emphasises the value of reaching sufficient coverage rates and community protection (also called herd-immunity[14]) in order to protect future generations. Nonetheless, there are currently numerous challenges across Europe and the world that delay access to vaccination.[4]

Challenges include, for example, rising vaccine hesitancy across the European Region, disparity in access to vaccination between and within countries due to fragmentation of European healthcare systems, the lack of infrastructures allowing performance evaluations of vaccination programmes,[15] and several regulatory restrictions.[16,17]

Today there is a unique momentum in Europe with significant engagement from the European institutions and policy-makers to fight against vaccine hesitancy and health-related consequences.[18] The introduction of the Joint Action on Vaccination (EUJAV) in 2018,[18] the Council Recommendation on *strengthened cooperation against vaccine-preventable diseases* in 2018,[19] the EU Roadmap on the implementation of activities against vaccine-preventable diseases in 2019,[20] and the 10 action points of the Global Vaccination Summit[21] are encouraging

* These infections are: tuberculosis, diphtheria, tetanus, pertussis, poliomyelitis, Haemophilus influenzae type B infection, hepatitis B, measles, mumps, rubella, pneumococcal disease, meningococcal disease, varicella, human papillomavirus infection (HPV), rotavirus infection, influenza, tick-borne encephalitis, hepatitis A

testaments of a shift in the political agenda towards a firm commitment to increasing vaccination coverage rates across the region.

However, as the former European Commissioner for Health Vytenis Andriukaitis pointed out in 2019, despite the numerous initiatives there are disappointing results. This is partially attributable to Member States watering down and softening a series of recommendations, particularly regarding innovation. The European Commission wanted to see firmer language in their recommendations. Consequently, there is a lack of ambition from Member States to implement the initiatives in a speedy and action-focused manner.[22]

> It's also time for the EU and its member countries to rethink where we failed, because there have definitely been failures, as seen in the 80,000 or so cases of measles in EU countries over the past few years
>
> Vytenis Andriukaitis
> former European Health Commissioner at the Global Vaccination Summit

In order to ensure the long-term sustainability of European healthcare systems, there is a need for efficient vaccination programmes and infrastructures,[23] enabling continuous innovation,[24] equity in access to vaccination,[25] and sustainable behavioural change.[26] Therefore, the objective of this report is to identify remaining pragmatic actions that can strongly support improved protection of the population through paediatric vaccination in the context of the life-course approach to vaccination, complementing the initiatives introduced by the EU institutions.

Methodology

The aim of this policy report is to identify gaps and opportunities in the current vaccination policy space in Europe. The research methodology for this report is based on comprehensive desk research, detailed data analysis, and targeted multi-disciplinary stakeholder interviews.

Desk research

Extensive desk research was conducted, which included reviewing publicly available literature on the topic of paediatric and life-course immunisation. This review included peer-reviewed articles, academic research papers and official reports. Additionally, this was complemented by targeted web-based research using search platforms and online portals.

Data analysis

The report also includes analysis of primary data on vaccination coverage and vaccine-preventable disease outbreak data. All datasets are taken from publicly available sources and referenced throughout the report.

Expert interviews

Semi-structured interviews with experts were conducted to validate and complement the findings of the research and analysis phases.

The full list of experts who contributed and a more detailed methodology, can be consulted in Annex I.

Why paediatric vaccination matters

Paediatric vaccination is a major driver in disease prevention. Since the first vaccine was developed in 1796, the number of available vaccines continues to grow. Today, we can effectively protect children from up to 18 infectious diseases.[6] Scientific progress in paediatric vaccination has helped significantly reduce the incidence of many childhood diseases. In June 2002, all 53 countries in the WHO European Region were certified polio-free.[5] A sustained effort of immunisation and disease surveillance helps maintain the Region's polio-free status and ensures that no polio case is undetected. Similar public health achievements could be envisaged for other vaccine-preventable diseases such as measles, rubella and other childhood diseases.[27] For example, the number of cases of Type C meningococcal disease in the UK has fallen by 90% in vaccinated groups since the introduction of MenC vaccines and by 66% in non-vaccinated groups due to the effects of herd-immunity.[28] Countries which have introduced the two-dose universal varicella vaccination have equally seen an up to 90% reduction in cases and associated complications, hospital stays, and deaths in all age groups.[29] Mortality due to vaccine-preventable childhood diseases has equally fallen. Measles-related deaths have decreased significantly since the introduction of measles, mumps, and rubella (MMR) vaccination programmes in 1968. It is estimated that, globally, over one in five of all child deaths are being averted thanks to the introduction of the MMR vaccine.[30]

Paediatric vaccination averts disease outbreaks

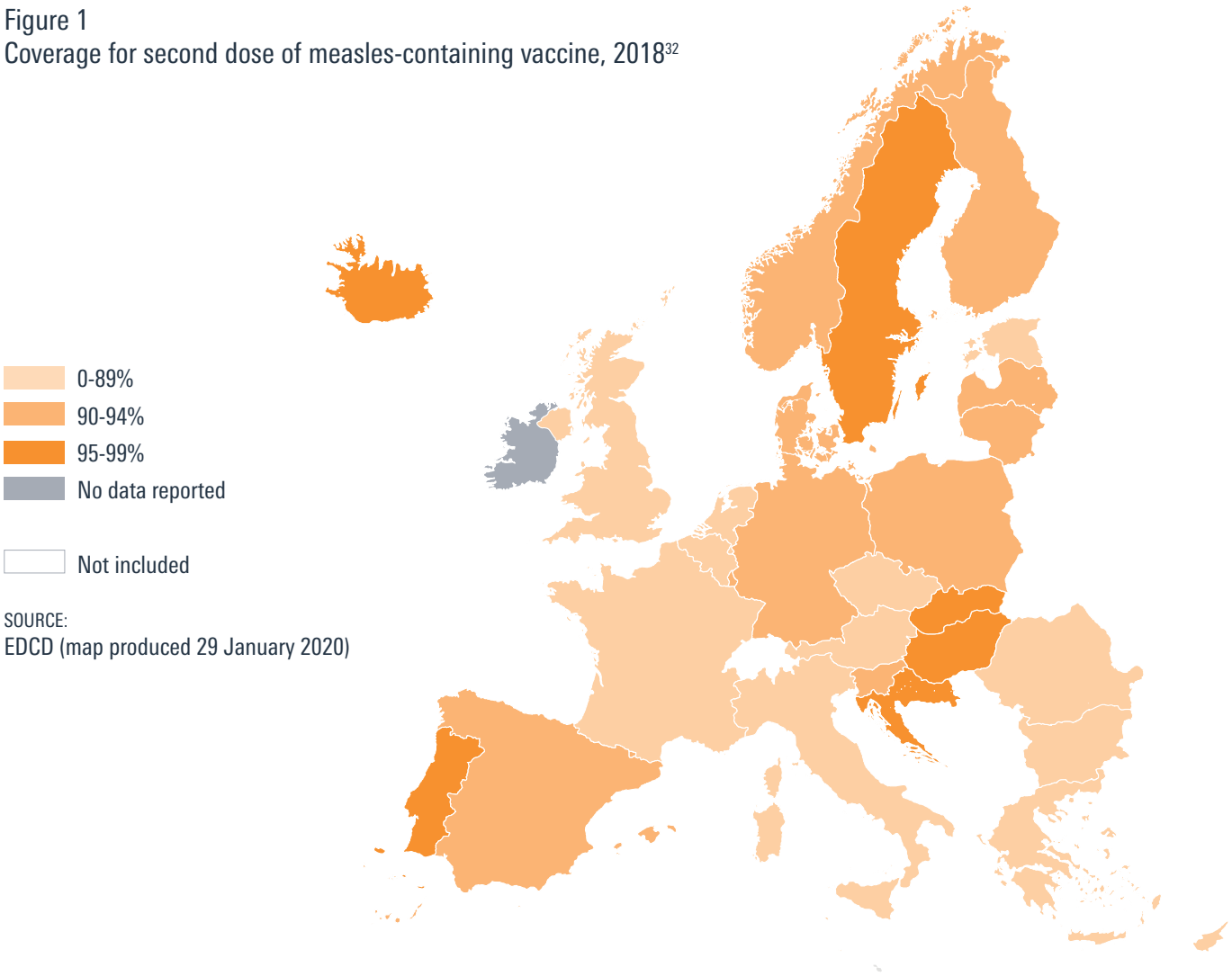
Despite previous successes and commitment to the European Vaccine Action Plan (EVAP) to ensure a European Region free of vaccine-preventable diseases – where all countries agree to provide equitable access to high-quality, safe, affordable vaccines and immunisation services throughout the life-course[3] – recent years have seen a decline in vaccine coverage rates.[4] Consequently, this has resulted in wide variation in protection of populations across Europe.[31] For instance, in 2017 only seven countries across Europe met the WHO recommended 95% coverage rate for the required two doses of measles vaccine.[15]

The direct effects of declining VCR are clearly reflected in the increase of disease incidence across Europe, with measles outbreaks at a record high.[33] In the 12 months between December 2018 and November 2019, there were 13,460 cases of measles reported across EU/EEA countries,[34] an increase from the 12,790 cases reported in the same period the previous year.[35] Similar trends can also be observed for other vaccine-preventable diseases such as rubella, where the number of reported cases in 2012 tripled compared to previous years.[36,37] The decrease in VCR is driven by a variety of factors including the growing role of technology in the rapid spread of misinformation,[38] complacency driven by the disappearance of many vaccine-preventable diseases,[39] and amplified vaccine safety, moral and ethical concerns amongst the population.[40] Additionally, the rise of populism and general distrust towards elites and experts increased mistrust in vaccination.[41]

Upholding the recommended coverage rate threshold is essential to enable herd-immunity (95% coverage for measles) through which the high proportion of the immunised population provides protection for those who have not developed immunity. When rates drop below this crucial threshold, vulnerable members of the population who cannot be vaccinated, such as children with immune deficiency or those undergoing treatment for diseases such as cancer, are dangerously susceptible to life-threatening infections.[42]

Given the cross-border nature of vaccine-preventable diseases and increase in migration and travel, diseases can easily spread across the Region. For example, the Ukrainian outbreak, with 57,000 measles cases in 2019 alone, has had a significant impact on the increased number of measles cases in Europe.[43] Therefore, it is essential that each EU Member State ensures sufficient VCR to prevent disease outbreaks.

Figure 1
Coverage for second dose of measles-containing vaccine, 2018[32]



SOURCE:
EDCD (map produced 29 January 2020)

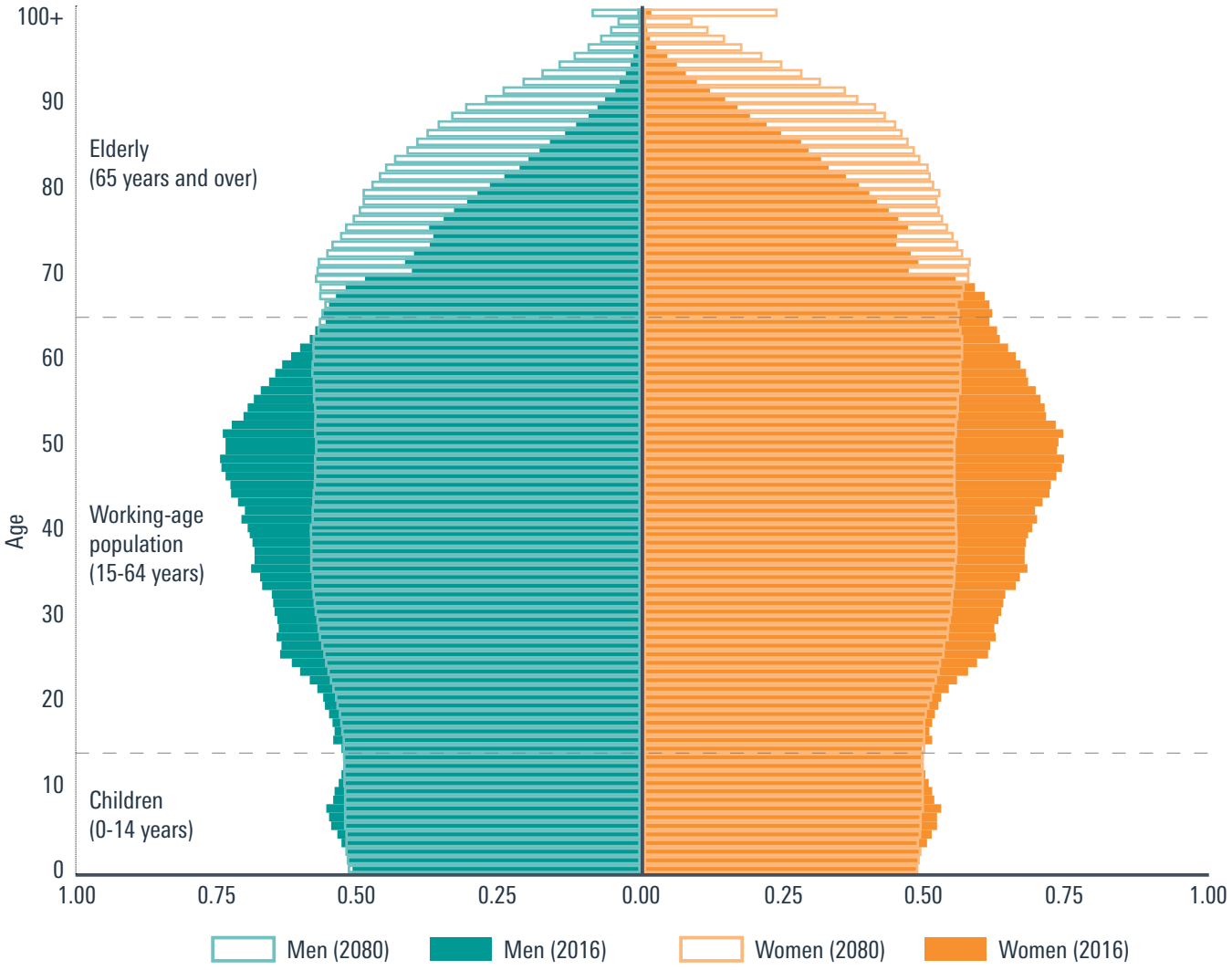
Paediatric vaccination as a first step in a life-course approach to vaccination

Currently, Europe is facing the challenge of an ageing population as life expectancy is increasing while birth-rates are decreasing. The current share of elderly people (65+) represents one fifth of the European population.[44] This is expected to increase to almost one third by 2080.[45]

To lower the burden on healthcare systems, older adults must be prevented from getting ill and vaccination is a key element of healthy ageing. At the same time, it is unaffordable to lose healthy young lives. Paediatric vaccination is a fundamental component of the life-course approach to vaccination and plays a key role in ensuring the long-term sustainability of European healthcare systems.

> Paediatric vaccination sets the standard from a psychological point of view: starting early has significant life-course implications
>
> Expert interview

Figure 2
2015: estimates, 2080: projections[45]



SOURCE: Eurostat (online data codes: demo_pjan and proj_150pms)

By protecting infants against infections and older generations against severe complications of infectious diseases, vaccination contributes to a reduced need for healthcare resources, freeing up hospital capacity for other life-threatening conditions.[46] By preventing illness in the population and reducing demand for healthcare resources, it has been estimated that vaccines can save society more than 10 times the original cost.[47]

Paediatric vaccination in the context of increasing AMR

By reducing the incidence of infectious diseases and thereby the need for antibiotics, paediatric vaccination also has a role to play in the fight against increasing AMR – which is one of the biggest global health challenges. This is notably the case in the prevention of pneumococcal bacterial infections or diseases inducing secondary bacterial infections such as varicella. By reducing the incidence of viral infections and associated bacterial complications, paediatric vaccination not only decreases the need for antibiotics but also the rate of inappropriate antibiotic use for viral infections.[48]

Vaccines – victims of their own success

In March 2019, the European Commission (EC) published results of a survey which examined the attitudes of citizens from the 28 EU Member States towards vaccination.* Noticeably, 48% of Europeans believe false claims on vaccines.[49] However, there are large differences between countries regarding the level of trust in vaccines. According to the survey, the main reason for not obtaining a vaccination is the thought that there is no need for it (34% of respondents), which was the most frequently selected response in 19 out of 28 Member States.*[49]

Vaccine hesitancy refers to a delay in acceptance or a refusal of vaccines despite availability of vaccination services. Vaccine hesitancy is a complex and context-specific concept, varying across time, place and type of vaccine. It includes factors such as complacency, convenience and confidence (as per the 3 C's Model) – as categorised by the WHO Vaccine Communications Working Group.[39]

Complacency

The decrease in the prevalence of vaccine-preventable diseases, such as polio or measles, has led to a decline in public perception of the severity of contracting those diseases. With fewer people having first-hand experience of polio or other life-threatening childhood diseases prevented by vaccination, there is a tendency to underestimate the probability of harm if a disease develops.[50]

> Very few people nowadays can imagine what it was like to have a brother paralysed by polio or lose a child at a very young age from meningitis. This achievement is also the biggest threat because it has removed the visual reminder of these infectious diseases so that parents – and even medical professionals – are much more at risk of underestimating these diseases
>
> Expert interview

Confidence

Despite the demonstrable impact of vaccination in reducing childhood illness and death, confidence levels have seen a worrying decline in recent years.[31] Misinformation often spread through social media is contributing to eroding trust and confidence, resulting in subsequent vaccine refusal.[51] A 67-country survey carried out by the Vaccine Confidence ProjectTM (VCP) in 2016 found that the WHO European Region has lower confidence in the safety of vaccines than any other region in the world.[31] A 2019 study by the Wellcome Trust showed that 33% of the population in France disagrees that vaccines are safe, the highest percentage of any country worldwide.[52]

Convenience

Despite the availability of safe and effective vaccines, lack of access to them is harming vaccine coverage rates worldwide.[21] The timing, availability and location of appointments have been identified as major logistical barriers to access to vaccination.[53] Additionally, there are missed opportunities to provide information on vaccines and to vaccinate individuals. These missed opportunities are attributable to, for example, lack of knowledge by the healthcare professional (HCP), insufficient appointment length or vaccine supply shortages. The WHO *Missed Opportunities for Vaccination* strategy recommends that any child or adult eligible for vaccination who visits a health service should be offered vaccination during that visit, no matter the reason for the visit.[25] In the UK, this principle is applied through the 'Make Every Contact Count' approach, which aims to ensure that every visit with a healthcare professional can be used to encourage healthier lifestyle choices, including immunisation.[54]

* The UK left the EU on 31 January 2020. There are currently 27 EU Member States.

> One of the biggest problems is access to vaccination, even when there is no hesitancy. It can be easy to forget an appointment or something similar. When you think about how many reminders we receive for an airplane flight or hotel booking – what if there existed a similar tool for vaccination?
>
> Expert interview

While different countries inevitably require tailored approaches to improve equity in access to vaccination,[25] increasing the range of providers who can administer vaccinations can increase opportunities for parents and children to access immunisation services.[15,53] Additional providers could include pharmacists, nurses, paediatricians and community health service providers. Convenience can be improved further through measures such as setting up a reminder system (e.g. by app, email, telephone call, post) for scheduled appointments[55] and the provision of flexible appointment times.[53]

In addition, there are also cost-related barriers which decrease access to vaccination. For example, where vaccines are not accessible free of charge, cost can be a substantial barrier, particularly for people who are unable to pay for vaccines out-of-pocket.[56] Healthcare systems offering universal vaccination free at the point of delivery can help overcome these financial constraints.[57]

Vaccination is one of the most economically effective public health interventions. No other health intervention can claim to be saving more than 10 times their original cost[47] or routinely protecting one individual for life against up to 17 infectious diseases (including preventing some cancers) for less than €3,400.[58] Nonetheless, currently Member States dedicate merely a small fraction – less than 0.5% – of their healthcare budget to immunisation. This is shown to be largely insufficient considering the level of investment that is necessary to provide the infrastructure that will inform and measure outcomes concerning the implementation of immunisation programmes. Therefore, there is a need for additional sustainable investment in vaccination infrastructures in Europe to ensure access and convenience for the population.[4]

Differences in recommendations and funding with regards to certain vaccines lead to inequality in access for European citizens. Additionally, this can induce confidence issues, as people may wonder why a vaccine might be made available in one country, but not in another one. Differences in recommendations across Europe entail e.g. the types of vaccines included in the vaccination schedule, the number of vaccine doses, the group to whom the vaccination is proposed, and the ages at which vaccines and boosters are recommended.[59] In addition, this can lead to missed vaccinations when people move across borders. To tackle this issue, public health authorities in the UK raised in 2019 the idea of listing MMR as a travel vaccine.[60]

CASE STUDY

Rotavirus (as of April 2020)

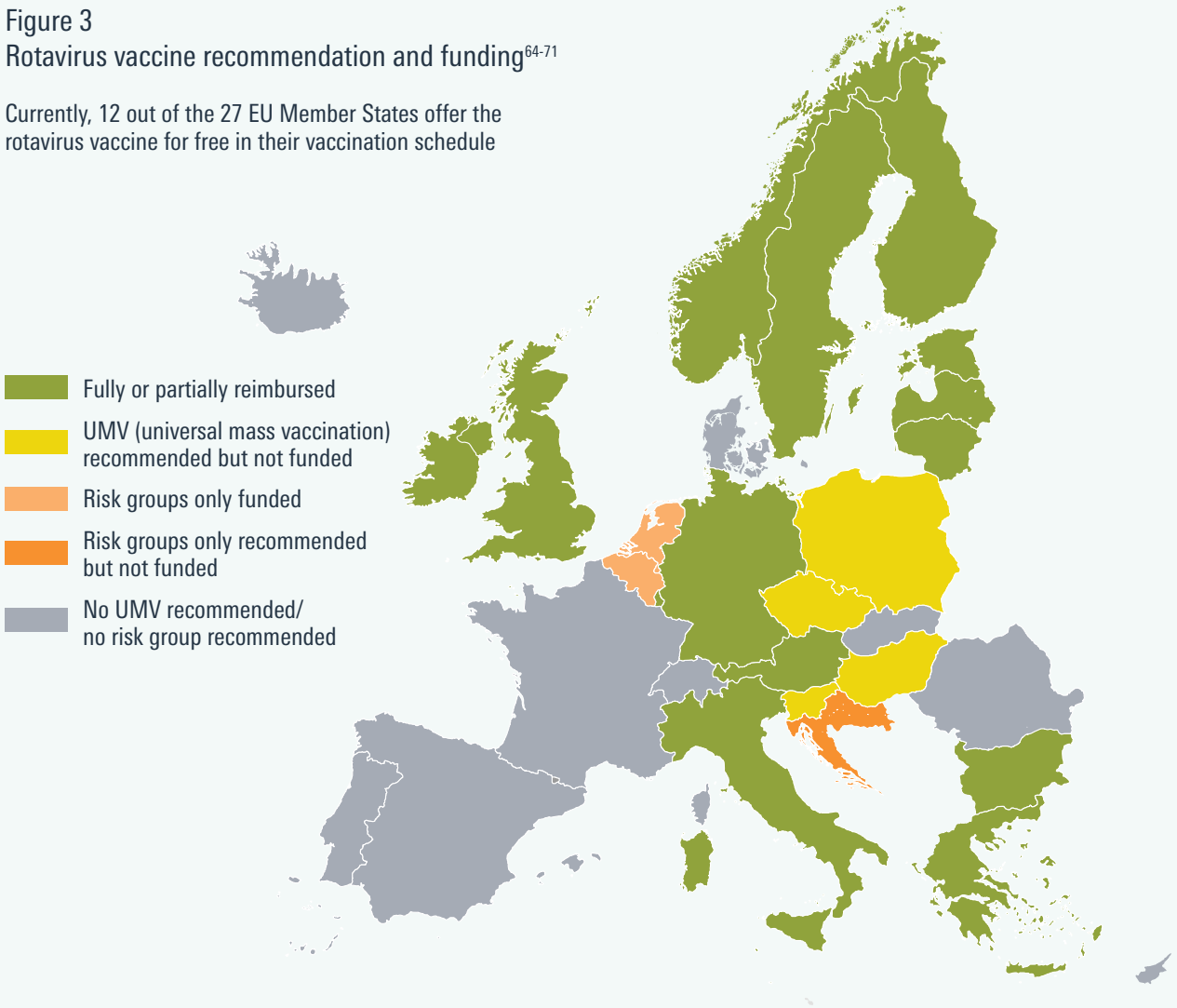
Rotavirus causes severe vomiting and diarrhoea in infants.[61] It is responsible for a third of hospital stays for severe diarrhoea in children under the age of five, accounting for approximately 75,000 to 150,000 cases per year across the EU.[62,63]

In countries with recommended and funded vaccination, hospitalisation rates due to rotavirus are reduced by 70-90% in <1-year olds.[64] This not only means less illness and better quality of life for children but also fewer days of work missed for parents, and reduced pressure on healthcare services. Research has shown that the rotavirus vaccination programme in Finland annually pays for itself at least two times over.[72]

Whilst a number of EU countries recommend the oral rotavirus for infants, substantial variation remains in the level of access across the region for a vaccine that is available since 2006.[64]

Figure 3
Rotavirus vaccine recommendation and funding[64-71]

Currently, 12 out of the 27 EU Member States offer the rotavirus vaccine for free in their vaccination schedule



CASE STUDY

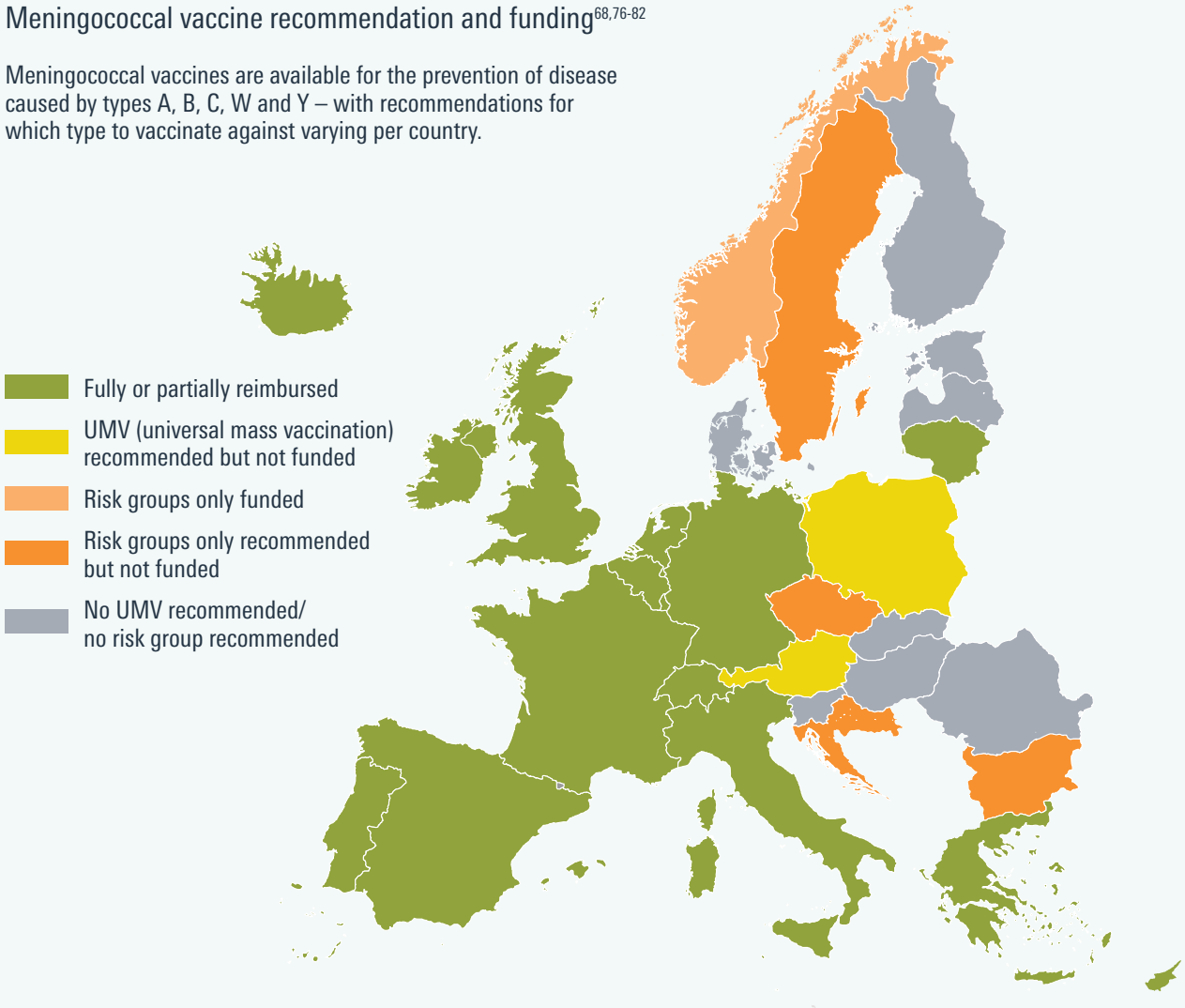
Meningococcal disease (as of April 2020)

Meningococcal disease can cause invasive meningococcal disease with meningitis and septicaemia, which is fatal in around 10% of cases.[73] It has many infectious causes, some of which are vaccine preventable.[74] Type B and C meningococcal are the most likely to cause invasive meningococcal disease,[73] for which effective vaccines have been available since 2013.[75]

Nevertheless, only 12 out of the 27 EU countries have included the vaccine in their national immunisation schedules for all children.[76] This leaves children and young adults exposed to serious and, in some cases, life-threatening infection.

Figure 4
Meningococcal vaccine recommendation and funding[68,76-82]

Meningococcal vaccines are available for the prevention of disease caused by types A, B, C, W and Y – with recommendations for which type to vaccinate against varying per country.



Strategies to reach sufficient vaccination coverages

As vaccine-preventable diseases do not adhere to borders, the EU institutions have recognised the importance of collective actions to tackle vaccine hesitancy, improve vaccination coverage and coordination between Member States, support research and innovation, and leverage innovative digital technologies across the Region.

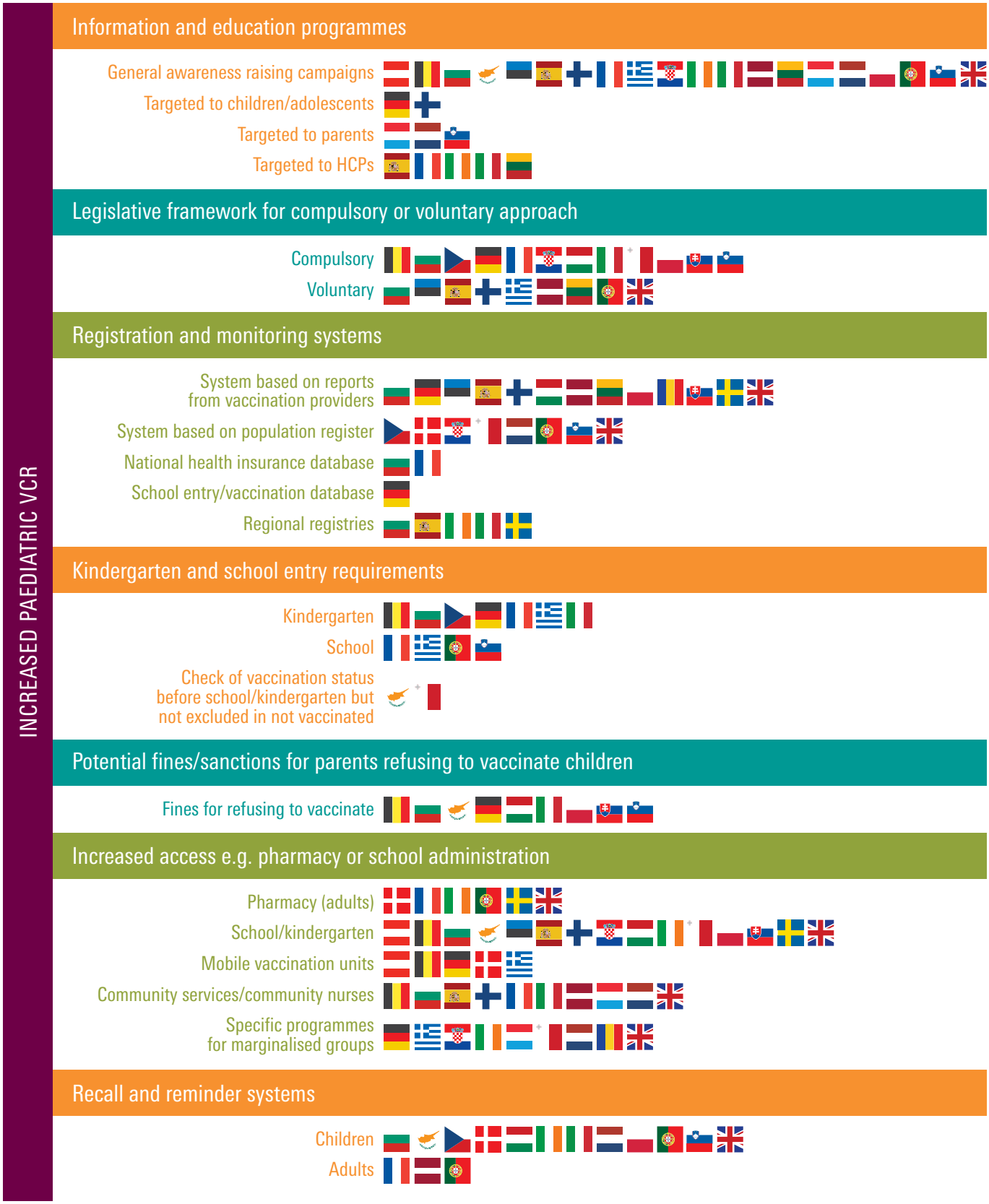
To this end, the European Commission's Roadmap for the implementation of actions in vaccination foresees several interrelated actions in the coming years. This includes the launch of a Coalition for Vaccination, assessing the feasibility of a European Vaccination Information Sharing system (EVIS), a proposal for a common vaccination card for all EU citizens, and steps to examine the feasibility of a core EU vaccination schedule.[20] However, it is essential to accelerate the implementation of the digital platform on vaccination and move rapidly from feasibility assessment to concrete actions and implementation to ensure citizens and healthcare systems can benefit from these innovations across Europe as soon as possible.

> There are significant differences between Member States, with each country having different guidelines and initiatives, which creates inequalities. We should take the best examples from each and translate this into concerted EU-level action to guarantee similar conditions for everyone
>
> Expert interview

National policy actions in paediatric vaccination

National governments across Europe have taken various approaches to increase paediatric vaccination coverage in their countries. These include for example implementing legislative frameworks (mandatory or voluntary), introducing recall and reminder systems, broadening opportunities for vaccination (e.g. through community-based providers), and launching information and education programmes and surveillance systems. Figure 5 presents the key national initiatives to drive paediatric vaccination coverage rate which are in place across the EU.[59,83]

Figure 5
National initiatives to increase vaccine coverage (see Annex II)



National case studies

Belgium's coverage rate for the first dose of the MMR vaccine is close to or above 95%. According to the WHO, one of the main reasons for this high coverage rate is that MMR vaccination is provided through public health services and primary health care providers, as well as paediatricians. Services are easily accessible, geographically well-distributed across the country, completely free of charge for the public health services and requiring only an administration fee when carried out by the paediatrician. Furthermore, staff members providing vaccines in well-baby clinics and school health services receive regular scientific and practical training. Uptake for the second MMR dose is, however, below 95% in all three regions, and below 80% in Wallonia and Brussels, where vaccine hesitancy is higher, fewer public health services are used and there are fewer catch-up modalities.[59]

Estonia is often cited as a best-practice example in digital developments (including in healthcare) and the country is a pioneer in electronic health records: every person who visits a doctor has an online e-Health record, including vaccination records. These records use KSI blockchain technology, meaning that a patient's electronic health information is kept secure but is accessible to authorised individuals.[84] Estonia is paving the way in digital health in Europe, for example with the cross-border exchange of e-prescriptions between Estonia and Finland which started in 2019. The 2017 Estonian presidency of the Council of the EU put e-health as a priority topic, with the 'eHealth Tallinn 2017' conference, as well as the launch of the Digital Health Society (DHS) Declaration – a call to action about strategies and actions to achieve digital transformation of healthcare systems.[85]

France is one of the most vaccine-hesitant countries in the world. Since January 2018, the country moved from 3 to 11 mandatory paediatric vaccinations. While there is no financial sanction system in place, non-vaccinated children cannot attend collective child services including nurseries and schools. The mandatory vaccination policy is intended to be temporary until public confidence in vaccines has been restored.[86]

In 2019, the French Health Minister attested rising vaccine coverage rates to the new policy, with 98.6% of children born between January and May 2018 having received the hexavalent vaccine,* up from 93.1% before the introduction of the new policy.[87]

Italy's national immunisation plan (2017-2019) aims to harmonise vaccination services across the regions.[59] The number of mandatory vaccinations was increased from four to ten, in response to a measles outbreak in the country in 2017.[59] Vaccination coverage rates subsequently increased in the first six months of 2018.[88] The most recent data from the Italian Ministry of Health shows an average measles vaccine coverage rate of 93.22%, up from 91.84% in 2017.[89]

Since September 2017, proof of vaccination is required for children under six years of age to enter nurseries and day care facilities. Older children are not refused entry into school, but parents receive financial sanctions.[59]

The Netherlands' national immunisation programme includes vaccination against 12 infectious diseases. While vaccination is not mandatory, over 95% of parents vaccinate their children.[90] Local vaccination centres provide easy access to vaccination services to encourage comprehensive uptake. Vaccination rates remain high among children under 10 years of age (data from 2017 to 2018), however there has been an overall drop of around 2-3% for most vaccinations since 2014. In the case of the HPV vaccination programme, the number of girls vaccinated has declined by 15% since 2016.[90]

The State Secretary for Health, Welfare and Sports announced a new plan in November 2018 to combat the decline in vaccination rates. One measure is to counter inaccurate information by setting up a team of independent experts who actively respond to misconceptions about vaccination, including on social media (e.g. by monitoring parents' questions, generating quick responses and correcting inaccurate or incomplete information).[91]

Sweden's children are offered protection against nine diseases through the national vaccination programme. Girls and boys are offered the HPV vaccine[6] and since 2016, all county councils also offer all infants vaccinations against hepatitis B. All vaccinations within the vaccination programme for children are voluntary and free of charge.[92]

The Swedish child vaccination programme has enjoyed a high rate of uptake for many years. Over 98% of children born in 2012 had been given at least three vaccine doses against diphtheria, tetanus, pertussis, polio and Haemophilus influenza type b, and over 97% of children were vaccinated with three doses of the pneumococcal vaccine. The percentage of children who had been vaccinated against MMR amounted to 97.5%.[93]

* The hexavalent vaccine protects against six diseases: diphtheria, tetanus, poliomyelitis, pertussis, Haemophilus influenzae type b, hepatitis B

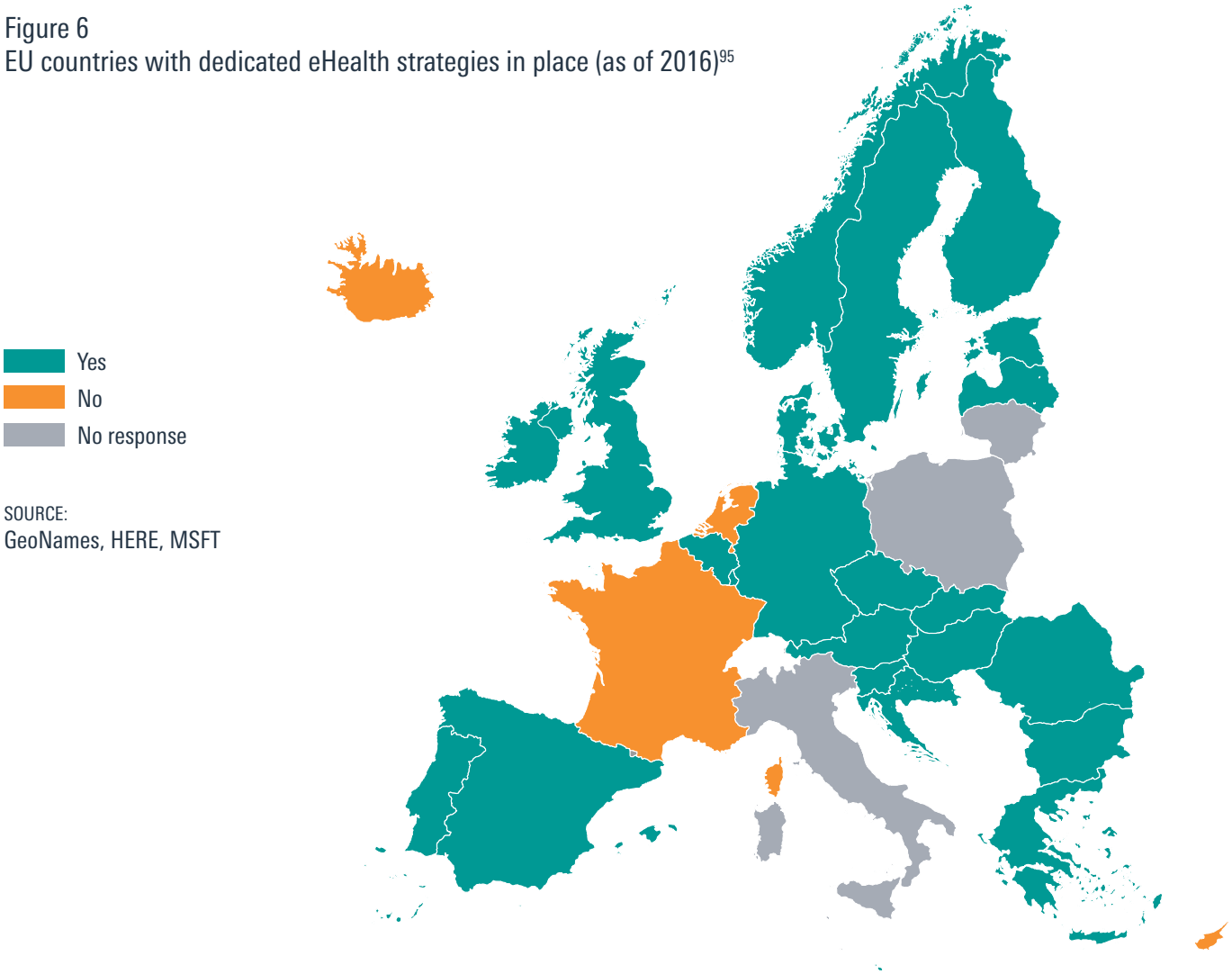
Digital technologies to support vaccination coverage

Digital tools can remind and incentivise uptake of vaccination, help study and track vaccine-preventable disease outbreaks and overcome practical barriers to visiting HCPs for information.

> It could be very useful to develop an app that helps parents remember the steps of a healthy child's development. This would include developmental milestones and reminders for vaccinations and doctor's checks and could inform parents about the severity of some diseases, which they don't always understand
>
> Expert interview

Digital technologies to improve immunisation programmes and coverage rates broadly fall into two categories: (1) decision support systems (e.g. reminders, delivery of information on vaccines including through social media) and (2) surveillance and data collection initiatives (e.g. immunisation registries, dose tracking, vaccine preventable disease surveillance, surveillance of adverse events, vaccine confidence monitoring).[94]

Figure 6
EU countries with dedicated eHealth strategies in place (as of 2016)[95]



SOURCE:
GeoNames, HERE, MSFT

While most European countries (23 out of 27 EU/EEA countries surveyed by the ECDC in 2017), have a dedicated eHealth strategy in place, only marginal progress has been made to integrate digital tools into immunisation programmes[95]

Vaccination uptake opportunities through digitalisation

The Council Recommendation on *strengthened cooperation against vaccine-preventable diseases* recognises that the lack of accurate information on vaccination in combination with the spread of misinformation has led to a significant decline in vaccine confidence across the region.[19] As a result, the EU recommends that Member States put in place strategies to increase the availability of scientifically accurate, comprehensible information to the public, including through use of digital tools.[19]

The European Commission recommends digital solutions to increase vaccination coverage:[20]

- A vaccination information portal to address safety concerns and fight vaccine hesitancy (2019)
- A European Information Sharing System to coordinate schedules (2019)
- An electronic vaccination card (proposal by 2022)
- Tailored e-learning tools (ongoing)
- A virtual EU data warehouse to tackle supply shortages (2022)

The European e-vaccination card could be an electronic health record that contains personal information about, for example, vaccination dates and dosage. Ideally, this would be a common vaccination card for EU citizens, which could be used by citizens and HCPs across borders. It would take into account different national vaccination schedules, be compatible with electronic immunisation information systems and be recognised for use across borders, without duplicating work at national level. This would provide opportunity to empower citizens, as they would be informed about their own vaccination status and have access to their own health data.[96] This in turn can lead to greater awareness and stimulate behavioural change in seeking vaccination amongst the European population.

In 2019, the WHO released its first guideline on digital health interventions setting out 10 recommendations for the use of digital technologies in health, including:[100]

- Sending appointment notifications via mobile devices through text, voice message apps or social media
- Digital tracking to support communication with patients, and establish decision support systems and e-Learning possibilities
- Adopting digital approaches to supply chain stock management

Electronic reminders can help increase adherence to vaccination schedules, especially if integrated with educational interventions.[97] The Austrian VaccApp is a vaccine education and empowerment tool which allows individuals to store vaccination records. A study carried out in Germany showed that VaccApp significantly improves parents' ability to keep track of their child's vaccination and can empower parents to take a more active role in providing accurate vaccination histories.[98] Another example is the French application MesVaccins, a public-facing phone app which allows people to easily input the vaccines they have received and find out immediately which vaccines they need, depending on their health status and environment. This provides them with an electronic resource which can remind them to get vaccinated, and which they can share with HCPs.[99]

A range of technologies are currently in research and development with the aim of increasing vaccine uptake, such as the use of vaccine-delivering nano-patches to minimise the use of needles and sophisticated algorithms to create personalised messaging.[101] Furthermore, the first human drug being developed solely by artificial intelligence – which is in the research and development phase – is a flu vaccine.[102] Additionally, artificial intelligence could also be used to spot potential outbreaks early, allowing HCPs and authorities to roll out targeted awareness raising and vaccination campaigns.[101] However, in order to benefit from these innovative developments, there have to be effective vaccination infrastructures in place to ensure access and correct implementation and evaluation of such innovations.

Surveillance, monitoring and data collection

Most European countries lack a system allowing for efficient implementation and close monitoring of immunisation programmes.[95] There is significant disparity in the use of digital technologies to provide the population with personal electronic immunisation records, provide HCPs with reliable vaccination histories for their patients, or provide Public Health Institutes with up-to-date coverage rates to analyse the efficiency of vaccination programmes. Immunisation Information Systems (IIS) are a tool that could address several of these needs and could potentially even unlock deeper clarification of the cause of declining VCR.

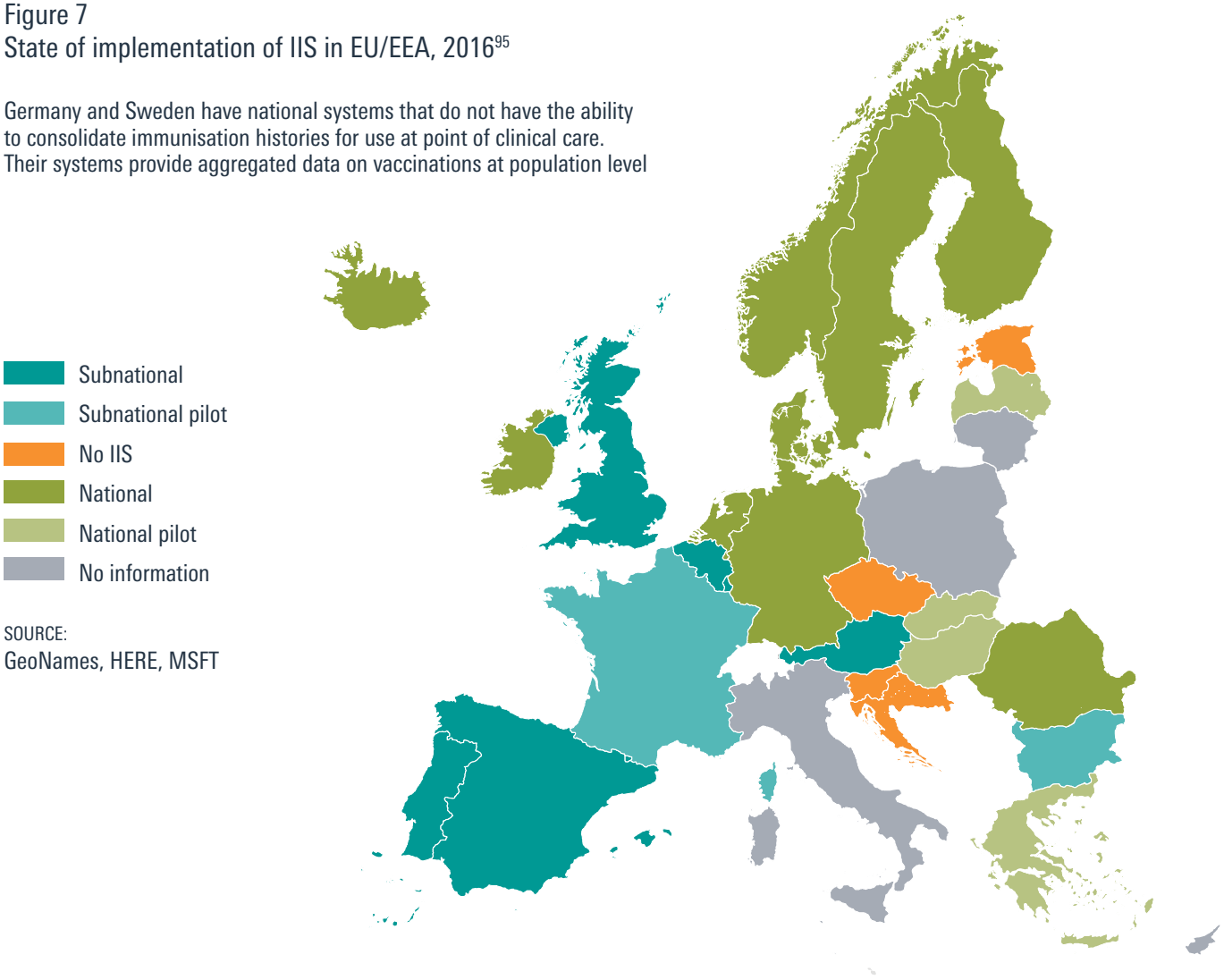
It is essential that citizens have access to their healthcare data to increase awareness and empower them to make better decisions about their health.[103] IIS could provide an effective tool for individuals to access their own, but also for example their families', vaccination status, potentially positively influencing adherence to national immunisation programmes.[104]

Additionally, IIS support physicians in their interaction with patients and enable the monitoring of vaccination rates across the population by recording, storing and providing access to high quality and timely data. IIS are key to ensure successful vaccination program implementation, to identify gaps and corrective activities, timely outbreak identification and response. Challenges that need to be overcome when establishing IIS include ethical considerations regarding confidentiality of health data and ensuring sustainable funding.[94]

Variations in the implementation of IIS persist across Europe. National systems for data collection are only in place in Denmark, Finland, Iceland, Ireland, Malta, the Netherlands, Norway, and Romania (figure 7).[95] The Nordic model – which gives a single identifying number to individuals, allowing for personal health information to be stored centrally – has been singled out by experts as the most advanced approach and should be considered for replication across the European region.[105] It is essential that IIS are correctly integrated in the diverse European health systems, ensuring that disease cases, adverse events after vaccination, and hospitalisation cases due to vaccine-preventable diseases are accurately recorded across the region.

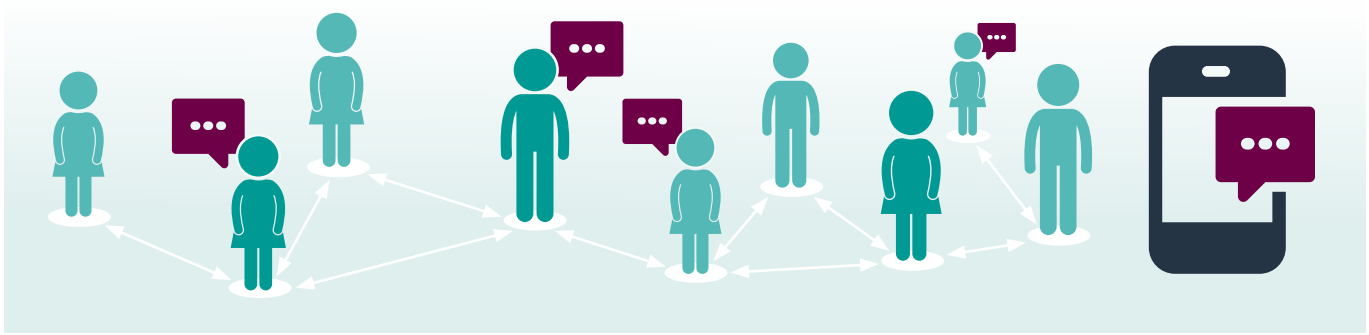
Figure 7
State of implementation of IIS in EU/EEA, 2016[95]

Germany and Sweden have national systems that do not have the ability to consolidate immunisation histories for use at point of clinical care. Their systems provide aggregated data on vaccinations at population level



SOURCE:
GeoNames, HERE, MSFT

In 2019, the Commission released recommendations to help facilitate cross-border information exchange through the European Health Record (EHR). The aim of the EHR is to allow citizens to securely access and exchange their health data anywhere in the EU.[106] The exchange of the EHR can help ensure that children's vaccines are not forgotten when moving from one country to another, for example, due to different vaccination schedules. In combination with electronic vaccine reminders which – through interoperable IIS – could operate across borders, this could be a significant step to ensuring that vaccines are not missed.



Social media and vaccination

Several social media companies are starting to take responsibility for the spread of fake news via their channels. Twitter in the UK redirects users searching for 'vaccines' to the National Health Service,[107] Facebook now limits visibility of anti-vaccination content,[108] Instagram emphasises to users using the search term 'vaccination' to consult trustworthy information and redirects them to the WHO website, and YouTube stopped serving ads to channels that spread anti-vaccine messages.[109] Social media initiatives at national level include the #ikvaccineer (#Ivaccinate) campaign in the Netherlands, in which medical professionals shared personal stories to explain why they and their children are vaccinated.[91] In Denmark, where HPV vaccination rates had declined following negative media coverage, organisations joined forces to disseminate information on the importance of vaccination on social media, resulting in an 100% increase in HPV vaccination rates in 2017.[91] In addition, reliable websites informing citizens about vaccination in Europe are active such as VaccinesToday.eu.

In order to reach policy-makers most effectively, it is important to align efforts by public and private stakeholders. For instance, redirection of social media users to the planned EU vaccine information portal could be a powerful way of countering misinformation and disseminating evidence, as would linking reminder services (e.g. by means of an app) to electronic vaccination cards.

Providing information on vaccines through social media can have a positive influence on parents' behaviours towards vaccination: a study on pregnant women showed that those who experience interactive information via social media are more likely to have their child vaccinated[110]

Training and education

Limited vaccination coverage among children can often be traced to a lack of understanding concerning the safety and importance of vaccination.[56]

The ECDC communication guide for HCPs *'Let's talk about protection: Enhancing childhood vaccination uptake'* highlights that healthcare providers are identified in multiple studies as the most important and trusted source of information for parents on vaccination.[111] Therefore, all HCPs providing vaccinations must be able to fully acknowledge parents' concerns and correct any potential misinformation.[56] In order to do so, it is essential they are trained and equipped to address any concerns parents may have around the effectiveness and safety of vaccines. One effective method of communicating on vaccination is **motivational interviewing (MI)**, which is a personal and directive counselling style designed to help reinforce a person's motivation to change their behaviour towards vaccination. It is common practice in Canada, where it helped to increase vaccination intention from 72% to 87%.[112] Similar initiatives could be considered across European countries.

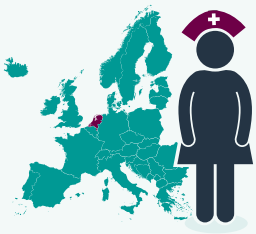
Motivational Interviewing (MI)

A personal and directive counselling style designed to help reinforce a person's motivation to change their behaviour towards vaccination.

CASE STUDY

Netherlands[113]

New parents receive a home visit from a nurse two weeks after the birth of their child, who informs them about the National Immunisation Programme and answers any questions. When their child is four weeks old, parents receive an invitation and information brochure about the National Immunisation Programme.



Additionally, the Council Recommendation on *strengthened cooperation against vaccine-preventable diseases* encourage Member States to strengthen training on vaccine-preventable diseases and immunisation in national medical curricula.[19] A cross-sectional nation-wide survey performed in France showed that education about vaccination in medical school in France is often sub-optimal, with one third of students feeling underprepared for questions on vaccination.[114] Similarly, vaccination education in German-speaking countries is reportedly low and often regarded as a minor subtopic.[115] Besides medical students, it is essential to ensure that other future HCPs who are in contact with the eligible population have the required knowledge and skills on vaccination, to inform, advocate or even administer vaccination themselves. These future HCPs can include nurses, pharmacists, and other specialists.

Engagement and education from an early age in life is also key in order to improve vaccine coverage rates among children and adolescents.[116] Parents can learn from their children and younger generations can drive change in behaviours. To this end, some educational initiatives across Europe aim to educate young people about the value of vaccination. These tend to be focused on online tools.

CASE STUDY

e-bug, 24 EU countries[117]

e-Bug is a free educational resource for classroom and home use to make learning about health issues fun and accessible. It includes lesson packs on vaccines and vaccination for primary and secondary school children.

Additionally, it has been suggested that organisations such as the WHO, ECDC and national health bodies could use social media platforms as a pathway to educate adolescents on the importance of vaccination.[118] However, to date, relatively little is being done to change attitudes towards vaccination in the long-term. Similar to other issues such as healthy eating, road safety or recycling, educating individuals about vaccination from a young age could allow for a long-term change in behaviour and attitude of future generations.[118]

> Education is the most important thing we can do to restore trust in vaccines. We have to start by educating children at school, embarking parents on the journey at the same time. Only with a combined approach including education can we hope to change preconceptions
>
> Expert interview

Empowering young generations

Another way to contribute to sustainable behaviour and attitude change towards vaccination is to involve youth directly.[119] Peer-to-peer interaction serves as an efficient foundation for knowledge transfer. Therefore, it is important to equip young health leaders with the knowledge and skills on how to communicate on vaccination. They can also serve as a bridge of knowledge between generations. Creating cross-generational transfer of knowledge can eventually lead to long-lasting changes in behaviour. Moreover, youth movements can influence political processes,[119] meaning that youth can have a significant impact on shaping the future of health in Europe, where prevention, including vaccination, plays a key role to ensure sustainability.

Supporting innovation in vaccination

There are several types of innovative vaccines. Among others, innovative vaccines include vaccines that protect against more than one disease, but also vaccines that are created using new techniques or against diseases that were previously thought not to be vaccine-preventable. Continued innovation in paediatric vaccines helps to reduce costs for healthcare systems and society, by i.e.:[120]

- Reducing childhood illness, mortality and long-term disabilities
- Reducing the days of work lost for parents
- Reducing the burden on healthcare systems

> It would be almost impossible to run the current immunisation programmes without combination vaccines
>
> Expert interview

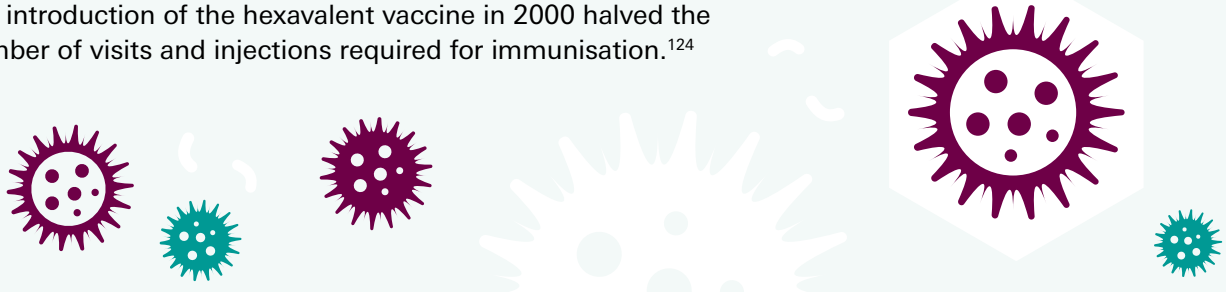
Continued innovation in vaccines has revolutionised our ability to prevent disease and improve public health.[121]

Since the first vaccine was developed against smallpox in 1796, the number of available vaccines continues to grow enabling us to protect children against up to 18 infectious diseases.[6] Some of these diseases have even been eliminated globally (smallpox) or in most parts of the world (polio). Vaccination is the only intervention that can claim to prevent infection-related cancers.[122]

Innovation in vaccines development also made possible to combine several vaccines in one injection.[123,124] The introduction of these combination vaccines reduced the costs related to medical visits required, improving compliance with vaccine schedules and increasing comfort for both parents and children.[124]

One shot to protect against six diseases

The introduction of the hexavalent vaccine in 2000 halved the number of visits and injections required for immunisation.[124]



Timeline of the first introduction or availability of main human vaccines

- 1796 Smallpox vaccine[125]
- 1885 First rabies vaccine[126]
- 1896 Cholera vaccine[127]
- 1921 Bacille Calmette-Guerin (BCG) vaccine[128]
- 1936 Inactivated influenza vaccine[127]
- 1946 Pneumococcal vaccine[129]
- 1955 First inactivated polio vaccine (IPV)[130]
- 1959 First oral polio vaccine (OPV)[130]
- 1963 Measles vaccine[131]
- 1967 Mumps vaccine[132]
- 1969 Rubella vaccine[133]
- 1971 Measles, mumps and rubella trivalent vaccine[134]
- 1974 First monovalent meningococcal vaccine (serogroup C)[135]
- 1974 Varicella vaccine[136]
- 1977 14-valent polysaccharide pneumococcal vaccine[137]
- 1981 Plasma-derived hepatitis B vaccine[127]
- 1983 23-valent polysaccharide pneumococcal vaccine (PPSV23)[129]
- 1985 Haemophilus b vaccine[138]
- 1986 Hepatitis B recombinant vaccine[139]
- 1998 Rotavirus vaccine[140]
- 2000 7-valent pneumococcal conjugate vaccine (PCV7)[137]
- 2000 First hexavalent vaccine (DTap-Hib-IPV-HepB)[141]
- 2005 Quadrivalent meningococcal vaccine[127]
- 2005 MMRV vaccine[134]
- 2006 Pentavalent rotavirus vaccine[134]
- 2006 Quadrivalent HPV vaccine[134]
- 2007 Bivalent HPV vaccine[142]
- 2010 13-valent pneumococcal conjugate vaccine (PCV13)[137]
- 2014 9-valent HPV vaccine[134]
- 2019 Ebola vaccine[143]

However vaccines – especially multi-component vaccines – are complicated to develop, and the manufacturing process requires strict and expensive quality control tests with a high failure rate of preceding efforts. Additionally, diverse regulatory requirements including WHO prequalification, national regulatory authorities' licensure and licensure in the country of use, combined with additional quality assurance and quality control requirements, are significant drivers of cost and require well-trained staff. Subsequently, on average, it takes between 12-36 months* to manufacture a vaccine before it is ready for distribution.[144]

However, it is important to acknowledge that access to innovative vaccines remains slow and heterogeneous across Europe. In EU Members States, it takes a median time of 6 years for a vaccine with market authorisation to become part of a national immunisation programme.[145] One of the reasons for this delay is the lack of harmonised clinical assessment of vaccines at EU, regional and national levels. Ensuring a European or joint clinical assessment, which is valid for all Member States, would reduce such redundancy and ensure timely access to innovative vaccines across Europe. A possibility to create this joined assessment is implementing a health technology assessment (HTA). However, the current platform is not suitable to address vaccines specificities yet. Vaccines are unique – they are preventative treatment to persons who do not have the disease and create herd-immunity. Therefore, it is complex to assess concretely the benefits of such intervention.

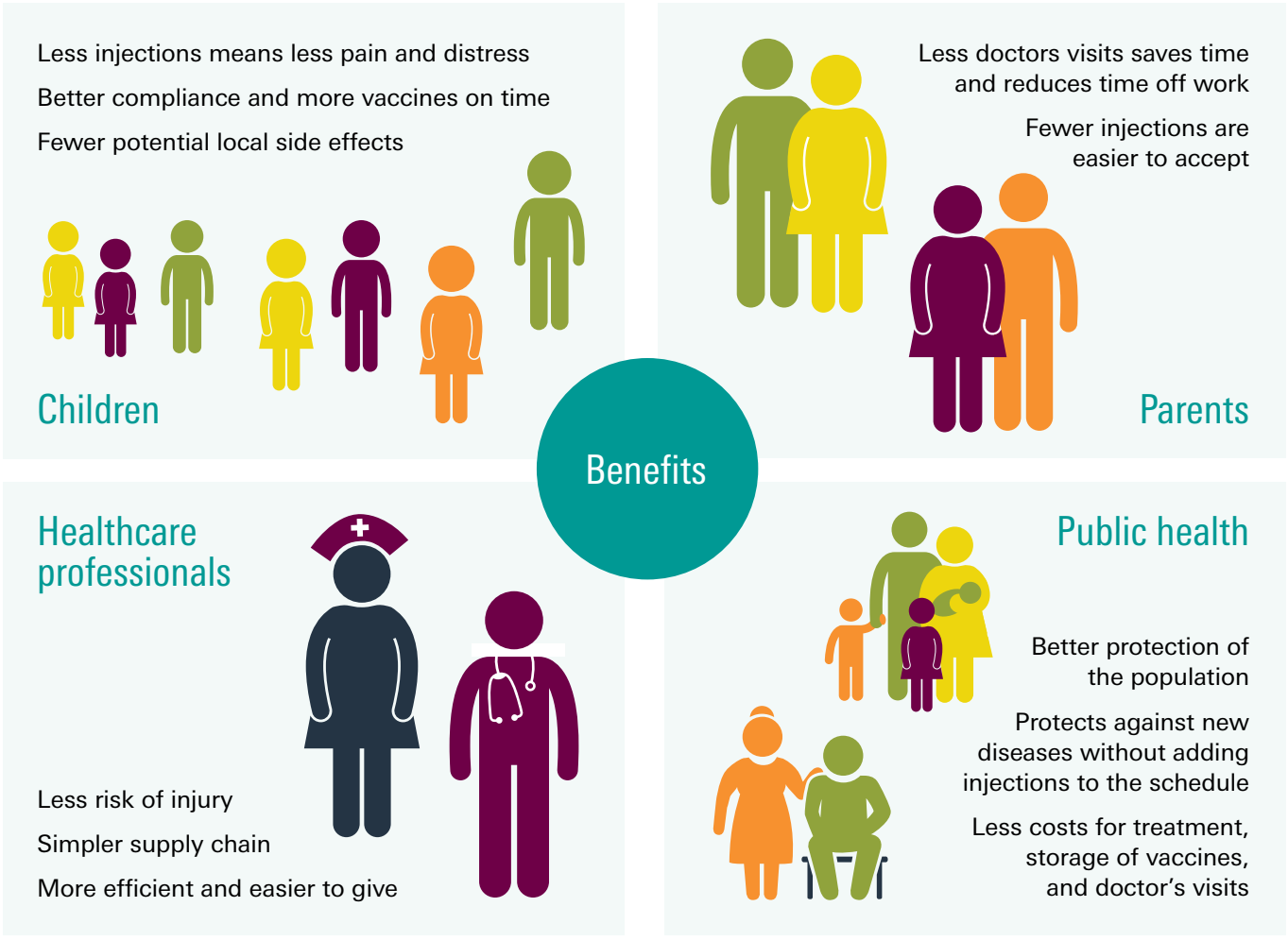
A specific and comprehensive framework for HTA of vaccines could be established in dialogue with key EU stakeholders, including the HTA Network and EUnetHTA. The aim would be to foster common good practices in method and evaluation throughout Europe to ensure rapid implementation of effective vaccination programs and ensuring evidence-based policy decisions.

It is essential that i.e. public health experts and National Immunisation Technical Advisory Groups (NITAGs), are fully involved in the clinical assessment.

*Complex multivalent vaccines can have production lead times of more than 36 months.

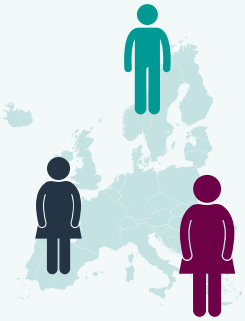
It is essential that researchers from the private and public sectors work together to develop new vaccines to help fight against global health challenges. The Council Recommendation on *strengthened cooperation against vaccine preventable diseases* calls on Member States to increase funding into vaccine research and development (R&D) in order to address existing unmet needs and identify priorities for future development.[19] Continued investment in R&D is needed to ensure the protection of future generations.

Figure 8
The benefits of combination vaccines[124]



Unlocking the full benefit of paediatric vaccination – Recommendations for policy-makers

This report makes the following recommendations to support policy-makers in their efforts to strengthen immunisation programmes allowing for life-long protection with successfully implemented paediatrics programmes across Europe:



Increasing access to available vaccines across the European Region

- Improve equity in access for European citizens by increasing coordination of vaccine decision-making across European healthcare systems, for example through the introduction of joint clinical assessment of vaccines at EU level
- Secure relevant level of funding for immunisation programmes to ensure sustainable service infrastructure, equity in access and continuous innovation in vaccination
- Increase the range of providers that can administer vaccination beyond the traditional settings to offer convenient access to vaccination for the population (e.g. including through schools, pharmacists, nurses, etc.)

Changing societal behaviour in a sustainable manner

- Ensure healthcare professionals have the latest knowledge and tools to advocate and advise on vaccination, for example through continuous education on vaccination, supporting them in addressing the public's concerns and effectively carrying out motivational interviews
- Introduce public health education programmes on vaccination as early as primary schools (as part of other prevention programmes e.g. around road safety or nutrition) to ensure generational change and embed vaccination as a social norm
- Engage and empower young generations to become active in vaccination allowing for cross-generational transmission of knowledge

Accelerating the use of digital tools and technologies

- Address regulatory, legal and financial barriers to accelerate the deployment of digital immunisation records across Europe
- Ensure the broad use of digital immunisation tools, not only for immunisation records but also for automated vaccination reminders for instance

Elevating the level of innovation in paediatric vaccination across the different components of the vaccine ecosystem

- Establish a best practice platform, highlighting different innovative approaches taken by European countries to encourage uptake of paediatric vaccination at the national level (e.g. kindergarten and school entry requirements or linking blockchain technology to electronic health records)
- Ensure innovation in vaccination is adequately valued and incentivised to encourage future research and investment, broadening the protection of the population against infectious diseases

Conclusion

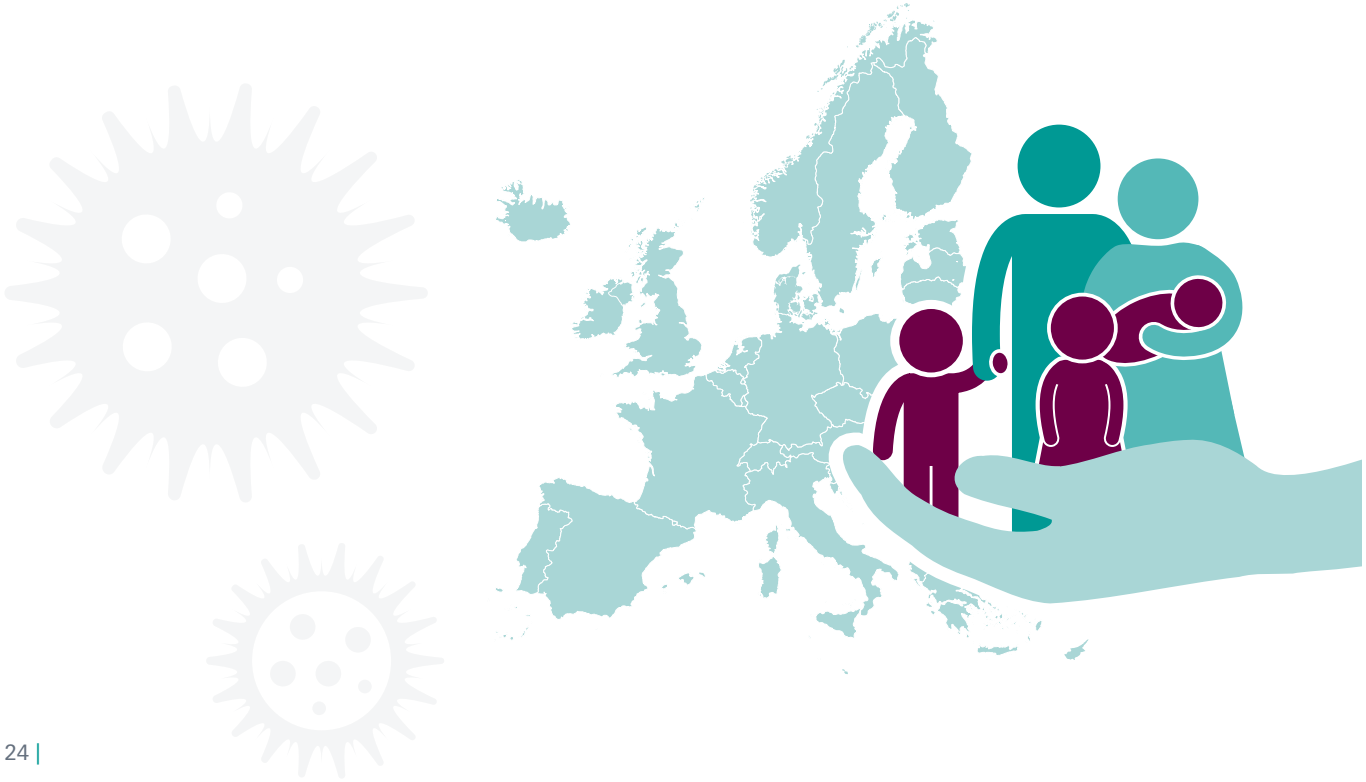
In order to improve protection of the European population against vaccine-preventable diseases, pragmatic actions are necessary. This means considering paediatric vaccination as an essential element in a broader life-course approach to vaccination and going beyond the current initiatives introduced by the EU institutions.

Paediatric vaccination is of tremendous value due to its direct and indirect positive effects on people's health and thus wealth. Nonetheless, coverage rates in Europe are failing and efficiency of immunisation infrastructures can be improved, emphasising the need to accelerate the use of digital tools and technologies. Besides innovation in the research, development and manufacturing of vaccines, it is essential to think innovatively about other parts of the vaccine ecosystem. Developing vaccines is not enough, citizens must have the intention and willingness to get vaccinated and sustainable infrastructures must be in place to ensure convenient access. Therefore, innovation in, for example, the way vaccination services are delivered, the way we communicate and educate on vaccination, the way data is collected and used, and the way innovation in R&D is supported, is crucial.

The time to leverage innovative opportunities to increase uptake – improving the long-term sustainability of European healthcare systems – is now. This requires bold leadership to ensure efficient vaccination programmes and infrastructures, enabling continuous innovation, timely and equitable in access to vaccination, and resulting in sustainable behavioural change across generations.

> The young population plays a key role in shaping the future perspective towards vaccination and therefore should be well-engaged.

Although many initiatives are taking place, there is room for improvement, especially in accelerating access to innovation including through digital solutions, educating and empowering youth, and ensuring national vaccination infrastructures are designed in a sustainable manner. Stakeholders must act together to ensure greater understanding of the unique value of paediatric vaccination across different generations. It is essential to unlock the full potential of paediatric vaccination, particularly in the context of current challenges such as an ageing population and antimicrobial resistance, in order to support European healthcare systems and protect the productivity and health of current and future generations.



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Annex I

Experts interviewed

- Dr Arnold Bosman, Director of Transmissible BV
- Dr Benoit Soubeyrand, Consultant in vaccinology, Blossom Vaccinology
- Professor David Salisbury, Associate Fellow, Centre for Global Health Security, Chatham House; former Director of Immunisation, Department of Health of the UK
- Mariano Votta, Responsible for EU Affairs at Cittadinanzattiva and Director of Active Citizenship Network
- Sam Nye, Executive Director, Confederation of Meningitis Organisations (CoMO)
- Professor Susanna Esposito, Paediatrician and Infectious Diseases Specialist, University of Parma, Italy

Interview methodology

Six experts in the field of paediatric and life-course vaccination were approached: six interviews were conducted over the phone and one interview was conducted in person, with one expert being interviewed twice over the phone. The interviews followed a semi-structured format over 50-60 minutes, covering a set of open-ended questions concentrating on key points to be covered in the policy paper.

Each interview was opened by introducing the project, explaining the objective of the interview and the reason for which that particular expert was approached, as well as gaining consent for their input to be included in the policy paper.

The interviews then followed a set of guiding questions, which fell under the following main subheadings:

- Adding value/topics and issues of interest
- Value of vaccines
- Value of paediatric vaccination
- Data and surveillance
- Vaccine hesitancy
- Perception of paediatric vaccination
- Innovation
- Antimicrobial resistance (AMR)
- Life-course vaccination
- Opportunities and challenges
- Examples of best practice or case studies

In order to ensure that the experts communicated their particular expertise organically, these questions were used to provide direction rather than as a strict guide and experts were encouraged to elaborate on certain points they felt were particularly relevant.

Methodology for desk research

The desk research included analysis of peer-reviewed articles, academic research papers, official reports, and other publicly available sources. Key words included: vaccination, immunisation, immunisation programmes, coverage rates, vaccination policies, vaccines, vaccine schedule, infectious disease outbreak.

Countries included in the analysis

The 27 Member States of the European Union:

- Austria
- Belgium
- Bulgaria
- Croatia
- Cyprus
- Czechia
- Denmark
- Estonia
- Finland
- France
- Germany
- Greece
- Hungary
- Ireland
- Italy
- Latvia
- Lithuania
- Luxembourg
- Malta
- Netherlands
- Poland
- Portugal
- Romania
- Slovakia
- Slovenia
- Spain
- Sweden

Other:

- Canada
- Iceland
- Norway
- Switzerland
- Ukraine
- United Kingdom

Paediatric vaccines included in the analysis

- Chickenpox (varicella) vaccine
- Diphtheria, tetanus, and pertussis vaccine (DTaP)
- Hepatitis A vaccine (HepA)
- Hepatitis B vaccine (HepB)
- Hib vaccine
- Human papillomavirus (HPV) vaccine
- Influenza vaccine
- Measles, mumps, and rubella vaccine (MMR)
- Meningococcal vaccines
- Pneumococcal vaccine (PCV)
- Polio vaccine (IPV)
- Rotavirus vaccine
- Tick-borne encephalitis vaccine
- Tuberculosis vaccine

Glossary

ACN
Active Citizenship Network

Antimicrobial resistance (AMR)
The ability of a microorganism (e.g. bacteria or virus) to stop an antimicrobial (such as antibiotics and antivirals) from working against it[1]

Combination vaccine
A single vaccine that protects against several germs in a combined injection[2]

CEF
Connecting Europe Facility

DHS
Digital Health Society

Diphtheria
A bacterial disease caused by the bacteria Corynebacterium diphtheria and Corynebacterium ulcerans: can cause lung symptoms or other forms that affect other parts of the body, including the skin (such as ulcers)[3]

ECDC (European Centre for Disease Prevention and Control)
The European Union agency aimed at strengthening Europe's defences against infectious diseases

EEA
European Economic Area

eHDSI
e-Health Digital Service Infrastructure

EHR
Electronic health record

Eradication of disease
The eradication of a disease is permanent and global, while the elimination of a disease is an achievement restricted to a specific geographic area[4]

EU
European Union

EVAP (European Vaccine Action Plan)
A WHO Europe regional interpretation of the Global Vaccine Action Plan developed to address the specific needs and challenges related to immunisation in the WHO European Region[5]

EVIS
European Vaccination Information Sharing System

Haemophilus influenzae type B (Hib)
A serious bacterial disease caused by the bacterium Haemophilus influenzae type B which can affect the lung and eyes, or produce widespread infection throughout the blood (sepsis) and meningitis[6]

Hepatitis A (HepA)
A viral disease caused by the hepatitis A virus (HAV). It is an acute disease, which can be mild or can cause fever, abdominal pain and jaundice. It does not cause chronic infection[7]

Hepatitis B (HepB)
A viral disease caused by the hepatitis B virus (HBV). Most people do not have symptoms with acute infection. After an acute infection, some people develop a chronic infection in the long term[8]

Herd immunity
When the vaccination of a significant portion of a population provides a measure of protection for individuals who have not developed immunity[9]

Hexavalent vaccine
A single vaccine that protects against six germs in one combined injection

Human papillomavirus (HPV)
A group of viruses which can cause abnormal tissue growth (e.g. warts). Long-term infection with certain types of HPV can cause cervical cancer,as well as playing a role in some other types of cancer[10]

IIS
Immunisation information systems

Influenza
Seasonal influenza is a viral disease caused by influenza viruses, which mainly causes respiratory symptoms. It usually occurs during the winter months[11]

KSI blockchain technology
A technology designed in Estonia and used globally to make sure networks, systems and data are free of compromise, while retaining 100% data privacy[12]

Life-course approach to vaccination
Vaccination given through all phases of life rather than focussing on discrete life stages (such as childhood)[13]

Measles
A viral disease which is capable of causing epidemics. It initially causes fever, conjunctivitis and respiratory symptoms, which is followed by a characteristic rash. It has a high mortality, which is usually caused by complicating bacterial infections[14]

Meningococcal disease
A bacterial disease caused by the bacterium Neisseria meningitidis. The bacterium usually lives in the nose and throat without causing disease, but invasive meningococcal disease is a major cause of meningitis and septicaemia[15]

MMR vaccine
A vaccine that protects against measles, mumps and rubella

Motivational interview
A patient-centred communication style used to enhance patients' internal motivation to change by exploring and solving their own ambivalences[16]

Mumps
A viral disease caused by the mumps virus. It usually causes inflammation of the parotid salivary glands, but can also cause orchitis (inflammation of the testicle), meningitis and pneumonia[17]

NIP
National Immunisation Programme

Nosocomial infection
An infection contracted in a hospital or other healthcare facility[18]

NVR
National vaccination register

Pathogenic agent
A biological agent that causes disease or illness to its host[19]

Pertussis (whooping cough)
A highly infectious bacterial disease caused by the bacteria Bordatella pertussis or Bordatella parapertussis. It causes lung symptoms, initially with cold-like symptoms, followed by the characteristic high-pitched 'whooping' cough[20]

Pneumococcal disease
A bacterial disease caused by the bacterium Streptococcus pneumoniae. Invasive pneumococcal disease is a major cause of death around the world[21]

Poliomyelitis
A viral disease caused by the polio virus. It affects the motor neurons, causing a spectrum of presentations from mild paralysis to death[22]

R&D
Research and development

Recombinant and conjugate vaccines
Vaccines that use only a specific part of the infectious agent and induce a very targeted response by the immune system[23]

Rotavirus
The most common cause of severe diarrhoeal disease in young children throughout the world[24]

Rubella (German measles)
A viral disease caused by the rubella virus. It is usually mild, but can cause severe foetal abnormalities if a pregnant woman is infected and the infection is passed on to the foetus[25]

Secondary bacterial infection
An infection that occurs during or after treatment for another infection[26]

Tetanus
A bacterial disease caused by the toxin of the bacterium Clostridium tetani. The disease is characterised by muscle spasms and is often fatal, especially in the generalised form[27]

Tick-borne encephalitis
A viral infectious disease that attacks the central nervous system and can result in long-term neurological symptoms, and even death. The virus is transmitted by the bite of infected ticks, found in woodland habitats. Initial symptoms include fever, fatigue, headache, muscular ache and nausea[28]

Tuberculosis (TB)
A bacterial disease spread from person to person through the air. Common symptoms include cough, chest pain, weakness, weight loss, fever and night sweats[29]

UMV
Universal mass vaccination

Vaccination coverage rate (VCR)
Percentage of the target population that has received the last recommended dose for a vaccine[30]

Vaccine-preventable diseases (VPD)
Diseases for which vaccines exist that can confer partial or complete protection[31]

Varicella (chickenpox)
A viral disease caused by the varicella-zoster virus. It typically affects children aged 2-8 years old, and usually causes cold-like symptoms, high temperature and an itchy blistering rash. If the virus is reactivated in adults it can cause shingles, with pain and a blistering rash in the area of the affected nerve[32]

VCP
Vaccine Confidence Project

WHO (World Health Organisation)
The United Nations specialised agency concerned with international public health

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All references last accessed in June 2020.

Annex II

Overview of national initiatives to drive paediatric vaccination coverage rate (VCR)

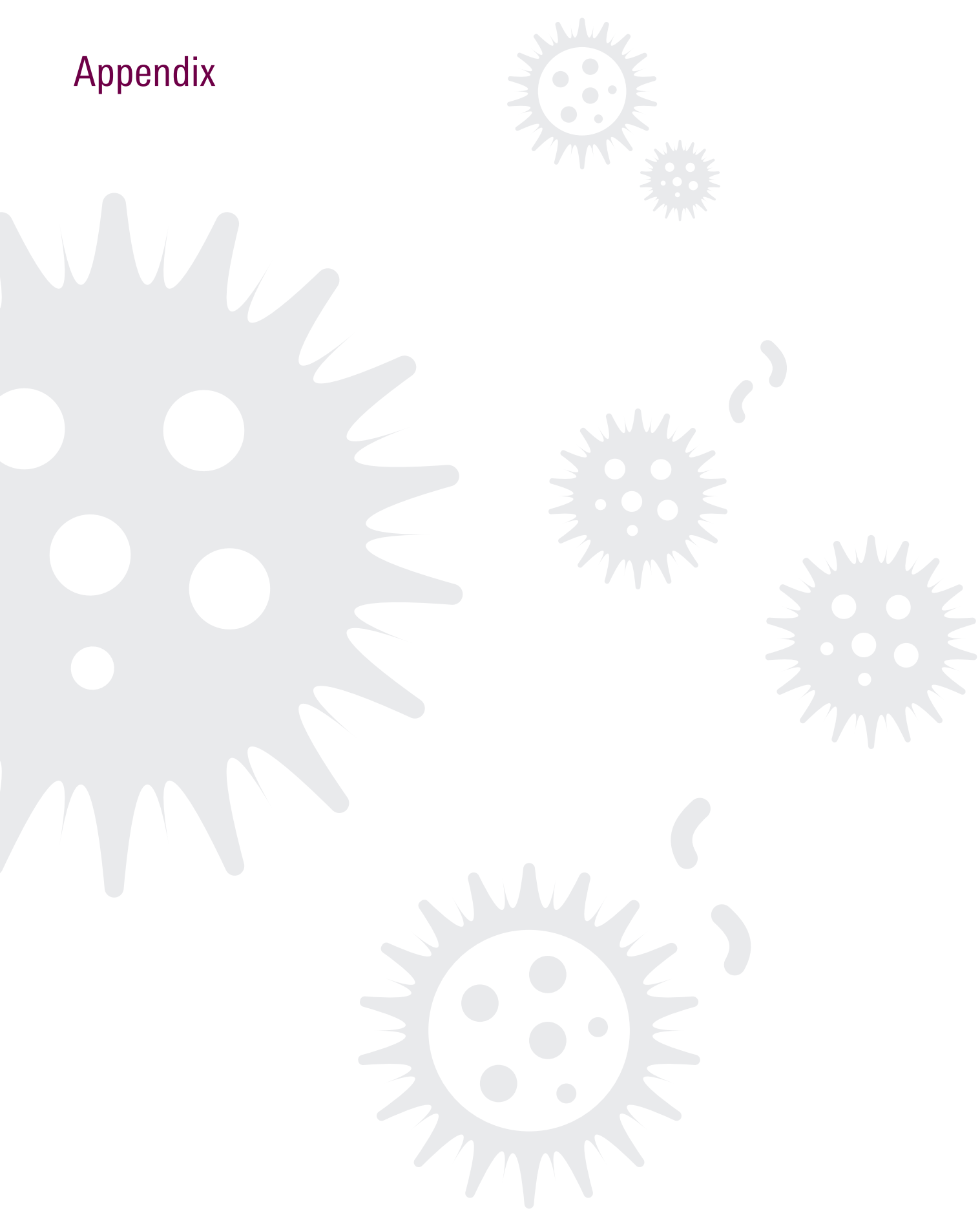
	AT	BE	BG[5]	CY	CZ	DE	DK	EE	EL	ES	FI	FR	HR	HU	IE	IT	LV	LT	LU	MT	NL	PO	PT	RO	SK	SI	SE	UK
Legislative framework for compulsory or voluntary approach																												
Compulsory		X[1]	X		X	X						X	X	X		X				X		X			X	X		
Voluntary/recommended			X			X		X	X	X	X						X	X					X	X			X	X
Registration and monitoring system																												
System based on reports from vaccination providers			X			X		X		X	X		X	X			X	X				X	X	X	X		X	X
System based on population register					X		X					X								X	X		X			X		X
National health insurance database			X									X																
School entry/vaccination database						X																						
Regional registries			X							X					X	X										X	X	
Recall and reminder systems																												
Adult vaccinations												X[2]		X			X						X					
Paediatric vaccinations		X[3]	X	X	X		X							X	X	X	X			X	X	X	X		X	X		X
Information and education programmes																												
General awareness-raising campaign	X	X	X	X				X	X	X	X	X	X		X	X	X	X	X		X	X	X	X	X	X		X
Parent-specific																			X		X					X		
Children/ adolescent-specific						X					X																	
HCP-specific										X		X			X	X		X	X									

	AT	BE	BG	CY	CZ	DE	DK	EE	EL	ES	FI	FR	HR	HU	IE	IT	LV	LT	LU	MT	NL	PO	PT	RO	SK	SI	SE	UK
Kindergarten and school entry requirements																												
Kindergarten		X[4]	X		X				X			X				X												
School									X			X										X			X			
Check of vaccination status before school/ kindergarten but not excluded if not vaccinated				X		X														X								
Increased access (e.g. pharmacy/school administration)																												
Pharmacy (adults)							X					X			X								X				X	X
School/kindergarten	X	X	X	X				X		X	X		X	X	X					X		X				X	X	X
Mobile vaccination services	X	X				X	X		X																			
Community vaccination services/community nurses		X	X							X	X	X		X	X	X	X			X	X							X
Specific programmes for marginalised groups			X			X			X				X		X				X	X	X			X				X
Local councils																				X								
Potential fines/sanctions																										X		
Fines for refusing to vaccinate		X[1]	X		X								X	X		X						X			X			
Fine for refusing counselling on vacination						X																						

1 polio 2 flu 3 polio by the commune 4 Wallonia 5 Bulgaria has both a mandatory calendar as well as a national immunisation programme (NIP) with a voluntary approach when it comes to rotavirus and HPV vaccination. The reminder system covers only the mandatory vaccines in general and eventually the subsequent applications of the NIP vaccines.

SOURCE:
European Observatory on Health Systems, The organisation and delivery of vaccination services in the European Union, 2018

Appendix



EXISTING UNMET NEEDS IN PAEDIATRIC VACCINATION

MSD INVENTING FOR LIFE

Vaccines save millions of lives around the world every day.[1] Through routine paediatric vaccination, people in Europe can be protected against up to 18* infectious diseases over the course of their lives.[2] However, there is still significant variation in access to paediatric vaccination across Europe, posing risks to children and society overall.

Rotavirus

A condition that causes vomiting and diarrhoea in babies[3]

It is responsible for 1/3 of hospital stays for severe diarrhoea in children under the age of five – 75,000-150,000 per year across the EU.[4]

Whereas many EU countries recommend the oral rotavirus vaccine for infants, substantial variation in the level of access remains across the region.[5-7]

In countries with recommended and funded vaccination, hospitalisation rates due to rotavirus are reduced by 70-90% in <1 year olds.[7]

Lack of access not only impacts young children but also:

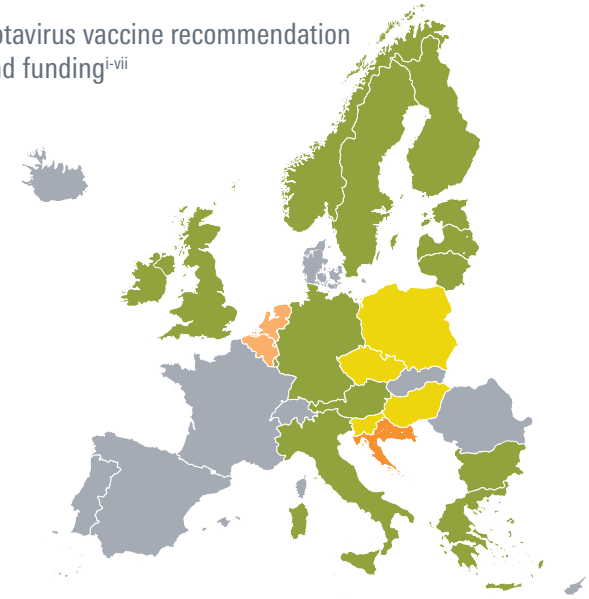
Families

Reduced quality of life and increased number of days-of-work lost[7]

Healthcare systems

Increased burden on healthcare professionals and number of hospital stays[7]

Rotavirus vaccine recommendation and funding[i-vii]

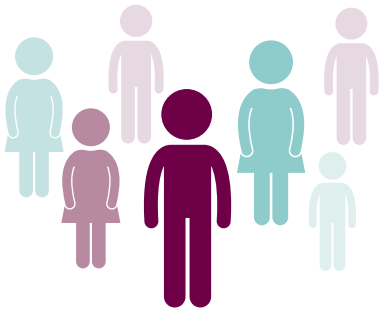


Currently 12 of the 27 EU Member States offer the rotavirus vaccine for free to all children in their vaccination schedule

CASE STUDY | GERMANY[8] Before being added to the national vaccination schedule, only some regions recommended the rotavirus vaccine, leading to large differences in coverage rates. As a result, the reduction in rotavirus related hospital admissions in children aged 0-1 year old varied by 41% between high and low coverage regions.

Varicella

A highly contagious viral disease commonly known as chickenpox



Varicella is a very common disease in Europe.

95% of infections occur in children under the age of 12.

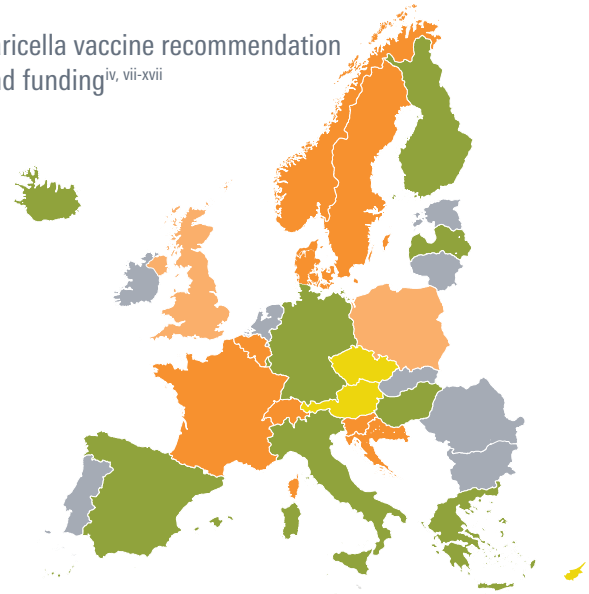
In a small proportion of cases severe complications can occur (including brain and lung complications, and in rare cases death).[9]

Currently, 8 of the 27 EU Member States offer varicella vaccination to all children for free within their national immunisation schedule.[10]

Yet varicella vaccines are highly effective:

Countries with 2-dose vaccination coverage have seen an up to 90% reduction in cases and associated complications.[11,12]

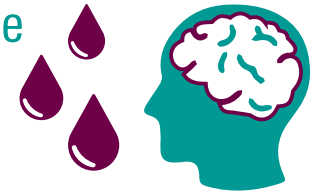
Varicella vaccine recommendation and funding[iv, vii-xvii]



High coverage rates have also helped reduce cases in unvaccinated people – helping to protect vulnerable people in society.[9]

Secondary bacterial infections can complicate varicella, but this can be prevented by vaccinating against varicella. This then reduces the use of antibiotics and thereby fights against the rise of antimicrobial resistance (AMR).[13]

Meningococcal disease



A serious disease, which is one of the causes of infectious meningitis

It can develop rapidly and be fatal in around 1 in 10 cases.[14]

It mostly affects children and teenagers.[14]

Meningitis has many infectious causes:[15,16]

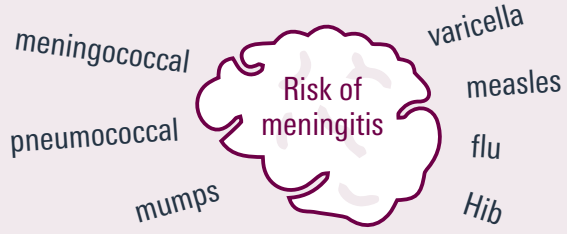
Bacteria

- Meningococcus
- Pneumoncoccus
- Group B streptococcus
- Haemophilus influenzae type b (Hib)
- Listeria
- E coli

Viral

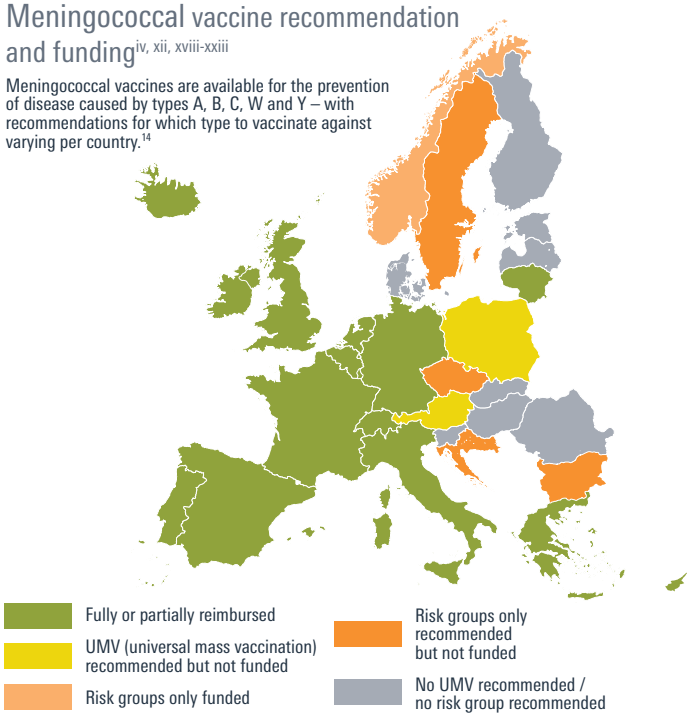
- Enteroviruses
- Herpes viruses: herpes simplex, CMV, EBV, varicella zoster
- Mumps virus
- Measles virus
- Flu virus

Effective vaccines exist for some:



Meningococcal vaccine recommendation and funding[iv, xii, xviii-xxiii]

Meningococcal vaccines are available for the prevention of disease caused by types A, B, C, W and Y – with recommendations for which type to vaccinate against varying per country.[14]



Type B and C meningococcus are the most likely to cause meningitis.

At the moment, 12 of the 27 EU countries offer meningococcal vaccination for all children free of charge in their national immunisation schedules.[17]

Lack of access to meningococcal vaccines leaves children and young adults exposed to serious and, in some cases life-threatening, conditions.

Addressing unmet needs

To ensure that people across Europe are protected against vaccine-preventable diseases, EU leaders have highlighted the importance of equal access to vaccination services regardless of geographical location.[18]

*These infections are: tuberculosis, diphtheria, tetanus, pertussis, poliomyelitis, Haemophilus influenzae type B infection, hepatitis B, measles, mumps, rubella, pneumococcal disease, meningococcal disease, varicella, human papillomavirus infection (HPV), rotavirus infection, influenza, tick-borne encephalitis, hepatitis A

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All references were last accessed in April 2020.

Date of last revision: June 2020

Job code: BE-NON-00433

KEY INNOVATIONS IN PAEDIATRIC VACCINATION

MSD INVENTING FOR LIFE

Scientific progress in paediatric vaccination

Vaccines save up to 3 million lives every year globally. Another 1.5 million deaths could be avoided if immunisation coverage around the world is extended.[1]

Paediatric vaccination can protect against up to 18* infectious diseases.[2] Due to advances in research, a new generation of vaccines protects against even more diseases, and makes existing vaccines more effective.[3,4]

Most Europeans are now protected against measles, mumps, rubella, diphtheria, pertussis, tetanus and polio. Protection against pneumococcal disease, human papillomavirus, hepatitis B and other infectious diseases is also increasing.[5]

Continued innovation in paediatric vaccines helps reduce costs for healthcare systems and society, by:

- Reducing childhood illness, mortality and long-term disabilities[6]
- Reducing the days-of-work lost for parents[6]

From smallpox to multivalent and combination vaccines

We have come a long way since Edward Jenner developed the first smallpox vaccine in 1796.

The introduction of combination vaccines reduced the number of injections and medical visits required, and the related costs, improving compliance with vaccines schedules and increasing comfort for both parents and children.[7]

The introduction of recombinant and conjugate vaccines in the 1980s further increased efficacy and helped to improve immune response of children and adults.[8,9]

What are.... ?[10,11]

Recombinant and conjugate vaccines
Vaccines that use only a specific part of the infectious agent and induce a very targeted response by the immune system, eg the Hib conjugate vaccine. Recombinant vaccines are produced through recombinant DNA technology and conjugate vaccines use a carrier protein to improve the immune response

Multivalent vaccines
A vaccine that protects against different strains of the same infectious agent, eg rotavirus vaccines can protect against up to 5 different rotavirus strains

Combination vaccines
A single vaccine that protects against several germs e.g. for diphtheria, tetanus, pertussis, poliomyelitis, haemophilus B, and hepatitis B, in a combined injection

Timeline

Date of first introduction or first availability to humans

1796	Smallpox vaccine[15]
1885	First rabies vaccine[16]
1896	Cholera vaccine[17]
1921	Bacille Calmette-Guerin (BCG) vaccine[18]
1936	Inactivated influenza vaccine[17]
1946	Pneumococcal vaccine[19]
1955	First inactivated polio vaccine (IPV)[20]
1959	First oral polio vaccine (OPV)[20]
1963	Measles vaccine[21]
1967	Mumps vaccine[22]
1969	Rubella vaccine[23]
1971	Measles, mumps and rubella trivalent vaccine[24]
1974	First monovalent meningococcal vaccine (serogroup C)[25]
1974	Varicella vaccine[26]
1977	14-valent polysaccharide pneumococcal vaccine[27]
1981	Plasma-derived hepatitis B vaccine[17]
1983	23-valent polysaccharide pneumococcal vaccine (PPSV23)[19]
1985	Haemophilus b vaccine[28]
1986	Hepatitis B recombinant vaccine[29]
1998	Rotavirus vaccine[30]
2000	7-valent pneumococcal conjugate vaccine (PCV7)[27]
2000	First hexavalent vaccine (DTap-Hib-IPV-HepB)[31]
2005	Quadrivalent meningococcal vaccine[17]
2005	MMRV vaccine[24]
2006	Pentavalent rotavirus vaccine[24]
2006	Quadrivalent HPV vaccine[24]
2007	Bivalent HPV vaccine[32]
2010	13-valent pneumococcal conjugate vaccine (PCV13)[27]
2014	9-valent HPV vaccine[24]
2019	Ebola vaccine[33]

Combination vaccines offer multiple benefits to children, parents and the healthcare system overall[7]

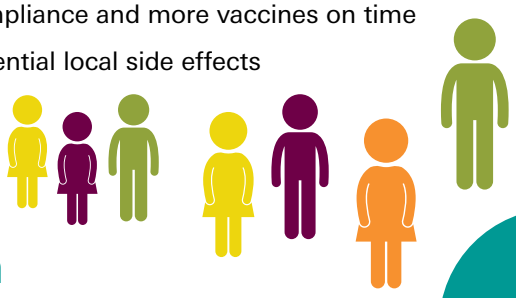
Benefits[7]

Children

Less injections means less pain and distress

Better compliance and more vaccines on time

Fewer potential local side effects



Parents

Less doctor's visits saves time and reduces time off work

Fewer injections are easier to accept

Healthcare professionals

Less risk of injury

Simpler supply chain

More efficient and easier to give

Public health

Better protection of the population

Protects against new diseases without adding injections to the schedule

Less costs for treatment, storage of vaccines, and doctor's visits

Challenges for development[7]

Complex vaccines formulation

Complex and long manufacturing process requiring strict and expensive quality control tests (i.e. consistency & reproducibility)

Difficulties in adjusting the level of vaccine components to minimize immune interference and still assure both efficacy and a favourable safety profile

Recognising the value of innovation to foster research in vaccination

Researchers from the private and public sectors are working together to develop new vaccines to help fight against global health challenges, including cancers and antimicrobial resistance.[12,13] Multicomponent vaccines can further increase protection and simplify vaccination schedules.[7] Continued investment in research and development is needed to ensure the protection of future generations.[14]

*These infections are: tuberculosis, diphtheria, tetanus, pertussis, poliomyelitis, Haemophilus influenzae type B infection, hepatitis B, measles, mumps, rubella, pneumococcal disease, meningococcal disease, varicella, human papillomavirus infection (HPV), rotavirus infection, influenza, tick-borne encephalitis, hepatitis A

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All references were last accessed in March 2020.

Date of last revision: June 2020

Job code: BE-NON-00457

TAKING ACTION TOGETHER ON MEASLES IN EUROPE

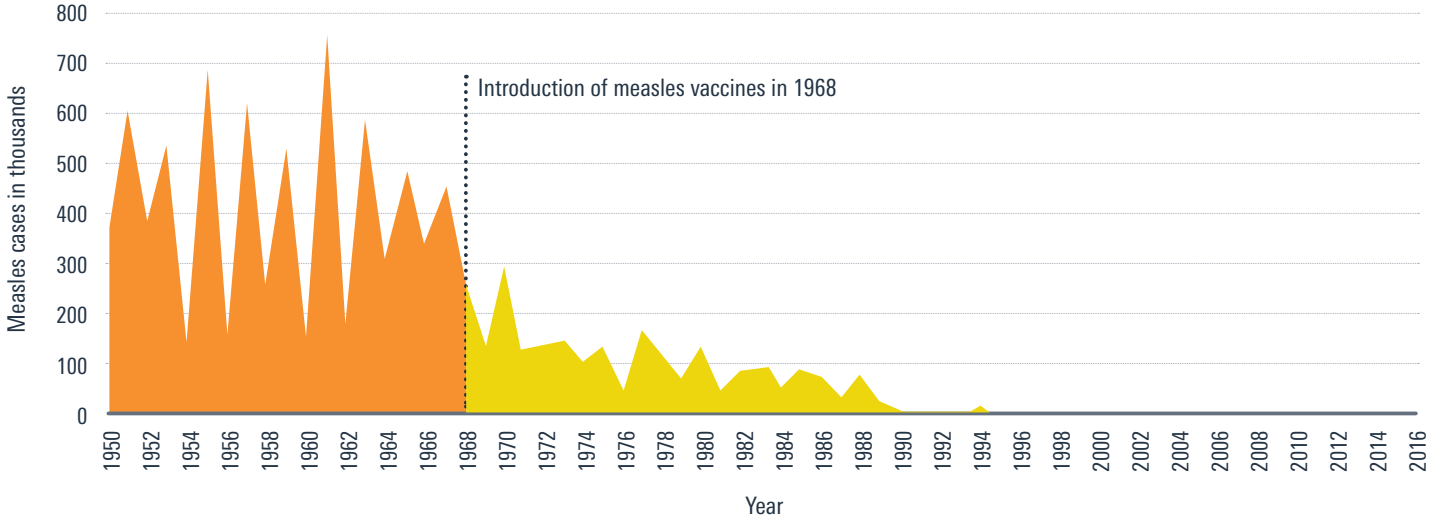
MSD INVENTING FOR LIFE

Measles – a serious but preventable disease

Measles is a highly infectious viral disease that can lead to serious complications, including infection of the lungs and brain. Yet it can be effectively prevented through vaccination.[1]

The introduction of measles vaccination in the 1960s has significantly reduced the incidence of the disease.[2] It is estimated that over 1 in 5 of all child deaths averted have been due to measles vaccination.[3]

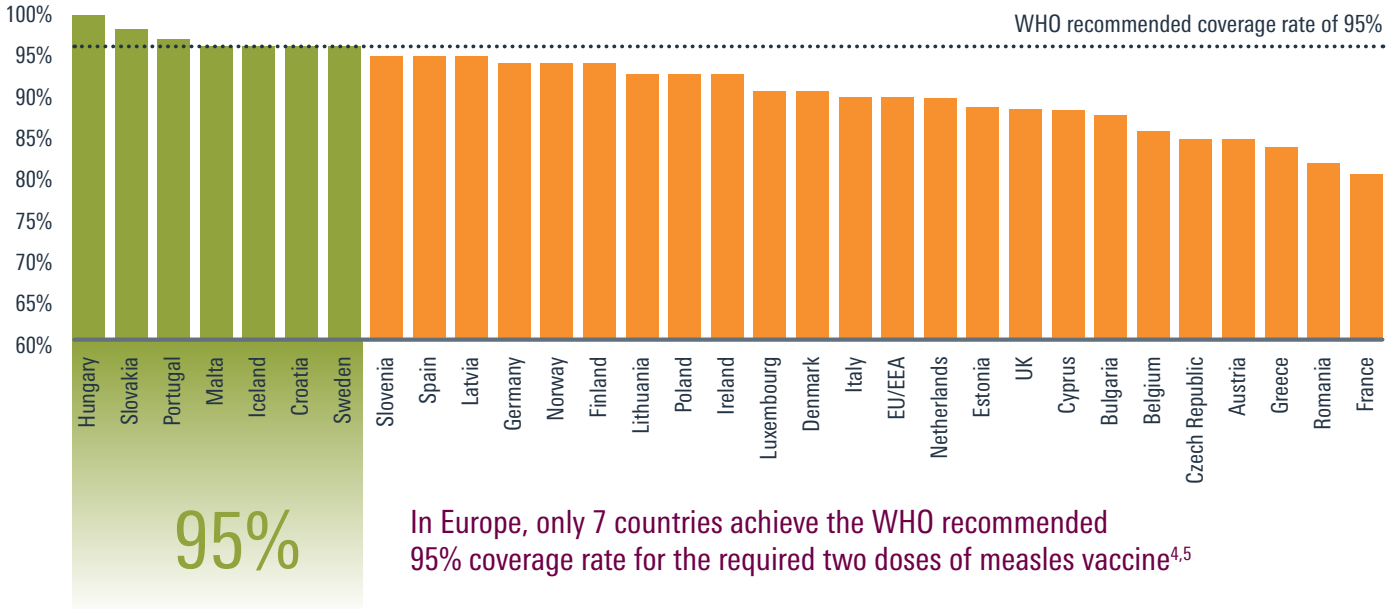
Development of measles notifications in England and Wales over time[2]



The importance of high vaccination coverage

The World Health Organisation (WHO) recommends high levels of vaccination coverage rates to ensure herd immunity in the population. Herd immunity helps protect those who cannot be vaccinated. Yet there is significant variation in coverage levels across Europe with France, Romania and Greece particularly lagging behind.[4]

Measles vaccination coverage (% of 2nd dose) in 2018[4]

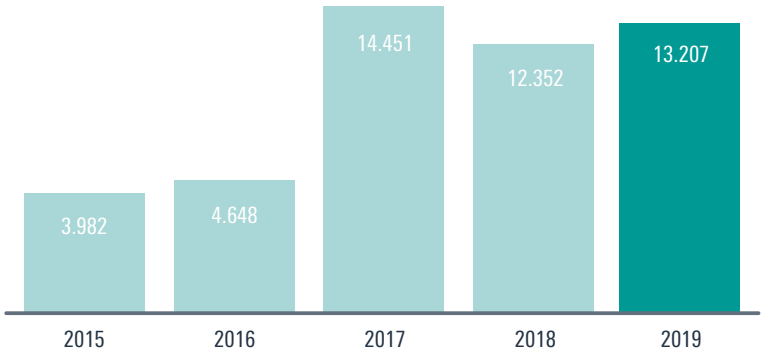


In Europe, only 7 countries achieve the WHO recommended 95% coverage rate for the required two doses of measles vaccine[4,5]

Measles outbreaks on the rise

Over 13,000 cases were reported across the EU/EEA in 2019 – more than 3 times that in 2015[6]

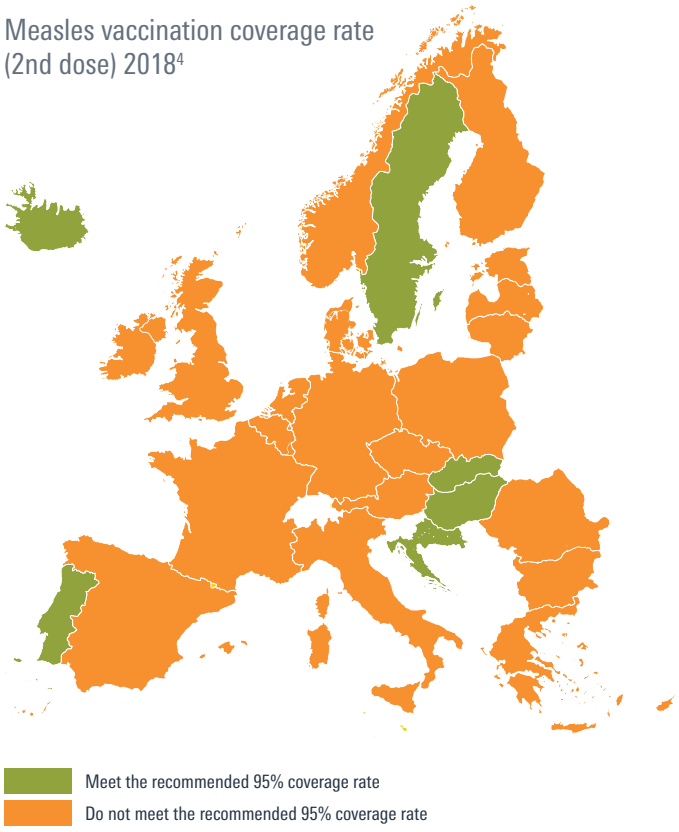
Number of measles notification (total) EU/EEA[6]



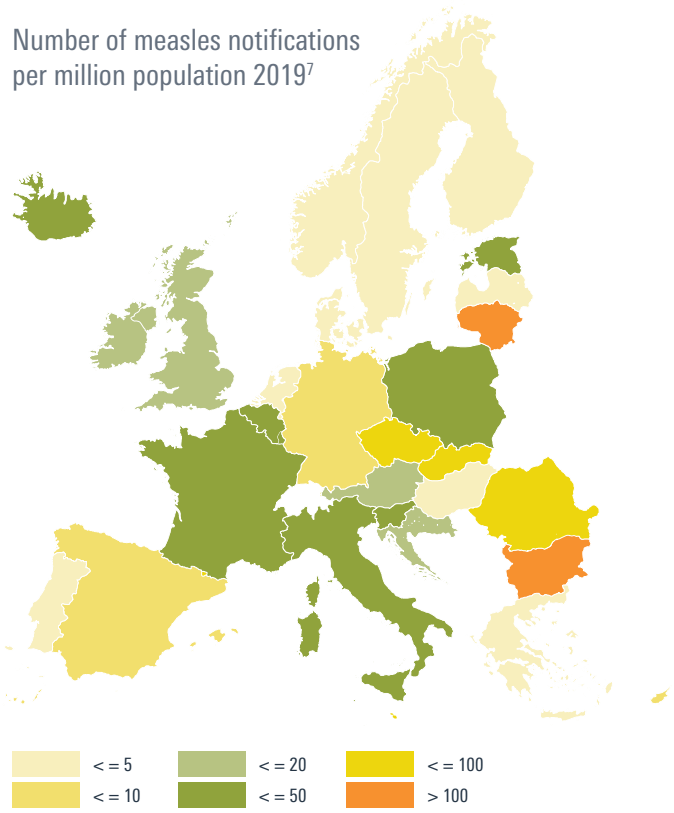
The level of measles outbreaks varies across Europe with Lithuania and Bulgaria particularly affected.[7] 10 deaths were caused by measles across Europe in 2019.[8]

The EU neighboring countries are severely affected with Ukraine experiencing over 57,000 measles cases in 2019 alone[9]

Measles vaccination coverage rate (2nd dose) 2018[4]



Number of measles notifications per million population 2019[7]



Paediatric vaccination policies across Europe

European countries have taken varying approaches to increasing uptake of measles vaccination, including reminder and recall systems, vaccination as a school entry requirement, targeted information and education programmes, and mandatory vaccination policies.[10] The implementation of comprehensive electronic immunisation records across all European member states is key to adequately monitoring coverage rates and running targeted vaccination programmes to avoid disease outbreaks.[11]

Taking action together

The time for action is now - EU leaders are calling for strengthened cooperation against vaccine-preventable diseases to achieve the required 95% coverage rate across Europe by 2020.[12]

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Date of last revision: June 2020

Job code: BE-NON-00451

This information is provided as a professional service by MSD. The views expressed in this publication reflect the experience and opinions of the authors and not necessarily that of MSD.

This report was drafted by Incisive Health based on desk research and interviews with leading experts in the field of vaccination. The contents have been approved by all listed as authors. Incisive Health would also like to thank those listed as contributors for their helpful inputs during interviews. The development of this report was initiated and funded by MSD. Experts were not paid for their time.

Date of last revision: October 2021

BE-NON-00466

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