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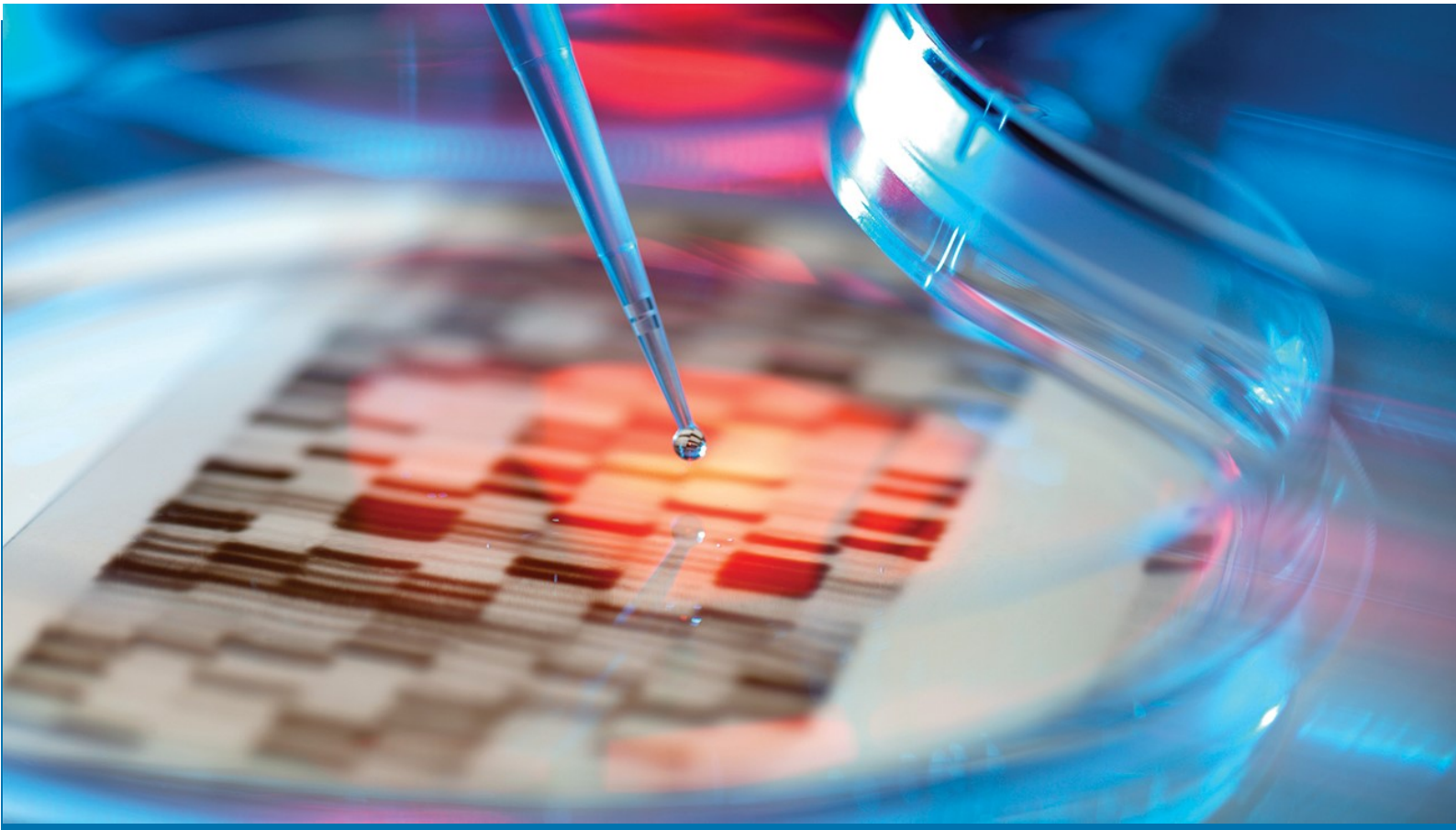

Policies to improve the Availability, Affordability and Access (the three ‘A’s) of Vaccines in Europe

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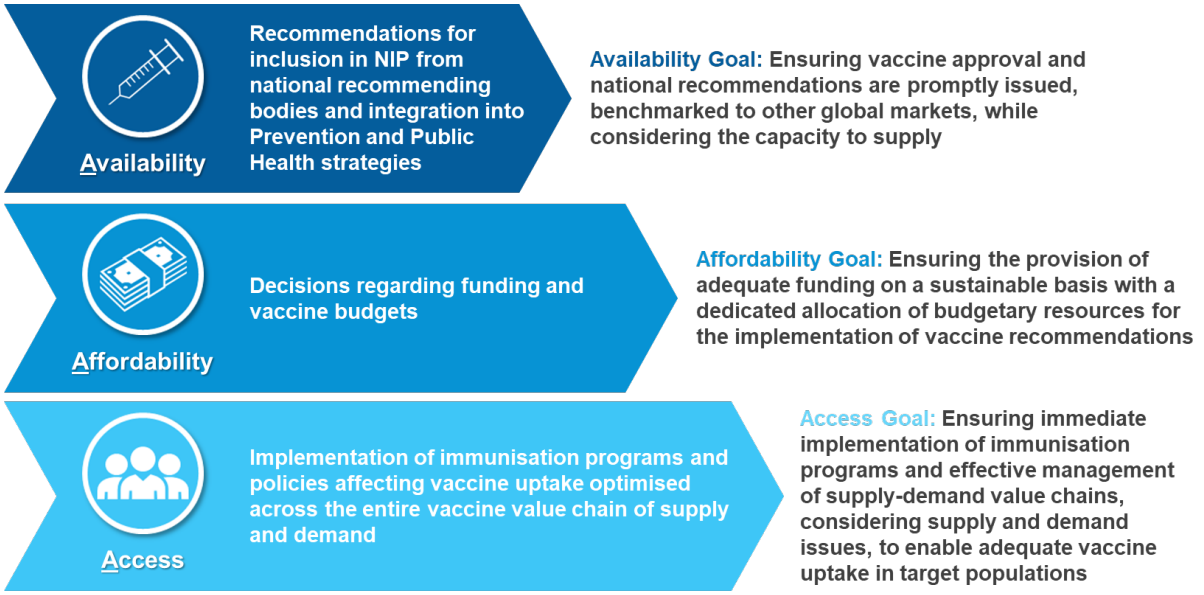
Executive Summary

Currently, vaccines can protect people against over twenty diseases and there is a rich pipeline of new vaccines in development.[1] However, there are significant differences in market access pathways across Member States and concerning issues in roles and decision-making criteria. The composition of National Immunisation Technical Advisory Groups (NITAG), critical in implementing National Immunisation Programmes (NIP), varies widely among countries. **Only 16 out of 22 European NITAGs** include the required specialists in vaccinology and immunology.[2] Despite the well-established, cost-effective role of immunisation in disease prevention, a staggering **77% of European countries spend less than 0.5% of their healthcare budget on immunisation**, with only a few increasing their budgets to adequately address their public health needs.[3] These constraints, among other issues, lead to delays, with some countries taking **more than 6 years for vaccines to become accessible**.[4] Consequently, there are discrepancies across Europe in terms of reaching target populations and achieving the recommended vaccination coverage rates.

Charles River Associates ('CRA') was commissioned by Vaccines Europe ('VE') to develop an analysis of the policy issues affecting the availability, affordability, and access (AAA) of vaccines in Europe. The aim was to define the three 'A's affecting routine vaccines, collect evidence on the cause of each of the three 'A's for the inclusion of these vaccines in NIPs, and how policy solutions could address these issues across the vaccine market access (VMA) pathway. In this context, routine vaccines refer to vaccines that are used as part of an ongoing, systemic vaccination programme including vaccines across the life-course. These findings have been tested and validated with various vaccine experts, including NITAG members, national payers, physicians, academics, and technical officers for the WHO.

Defining availability, affordability, and access for vaccines

The three 'A's—availability, affordability, and access for vaccines—have received more attention following the COVID-19 pandemic. A conceptual framework was developed with VE members including a definition of each of the A's, an associated goal, and showing the **interdependency of the three A's by presenting them as a cascade, rather than a strictly linear pathway**. This is a simplification, as, in reality, decisions in European countries can occur in parallel, overlapping across areas. For example, budgetary discussions may happen concurrently with NIP considerations. However, if the goal for the three A's were reached this would **support optimal vaccine uptake across Europe**.



Underlying causes of differences in availability

Vaccine availability is dependent on securing market authorisation by the relevant regulator (the European Medicines Agency (EMA) in Europe) after which manufacturers must then undergo individual national assessment for the vaccine's inclusion in the NIP. Key steps at the national level may include horizon scanning, early advice, NITAG assessment, and recommendations for consideration of vaccines into NIP. The underlying causes of differences in availability include:

- Delays to marketing authorisation and the timeliness of regulatory revisions
- Lack of early and continuous dialogue from recommending bodies with industry to better anticipate NITAG review timelines, HTA review procedures and demand planning for new and existing vaccines
- Misalignment of evidence requirements and evidence value due to varying healthcare system processes
- Heterogenous national assessment systems with limited life-course vaccine prioritisation and lack of transparency with vaccine manufacturers and the public
- Restrictions in the recommended target population due to the influence of budgetary concerns rather than public health considerations

Underlying causes of differences in affordability

The funding provisions for immunisation programmes need to adapt to reflect the introduction of new vaccines. The underlying differences related to affordability are driven by the availability of budget to facilitate the implementation of vaccine recommendations including:

- Insufficient budget allocated for effective implementation of NIPs to fulfil the needs of target populations
- Inability of budgets to have the flexibility to adapt to the changing public health needs and ongoing vaccine innovation
- Lack of alignment between national and regional decision-makers on public health priorities and budget allocation

Underlying causes of differences in access

The underlying differences in access relate to the effectiveness of implementing national immunisation programmes and supporting enablers that result in optimal uptake of vaccines in target populations. The underlying causes of differences in access include:

- Procurement practices that reduce market attractiveness and limit supply adaptability to evolution of population needs that do not account for overall vaccine manufacturing challenges
- Limited expansion of vaccination access points for effective implementation of life-course immunisation to support equitable access
- Differences in guidelines and involvement of HCPs in vaccine administration
- Policies affecting equity and individual patient affordability, e.g., co-payments
- Lack of infrastructure to collect, monitor and evaluate RWE to support appropriate vaccine uptake in target populations, limiting VCR
- Lack of comprehensive education for HCPs and the public, increasing vaccine hesitancy and hindering acceptance of new vaccines

Policy opportunities

Given the multifactorial root causes, the need for a dialogue on how to improve the three 'A's for vaccines is clear. Drawing on the key findings and supporting evidence of factors affecting the three A's, we identified a number of opportunities to improve the policy environment to address the underlying causes of differences across the three 'A's. Given the multifactorial root causes, there is a need for a multi-stakeholder dialogue on how to improve the policy environment. Only by addressing the underlying causes of variation in availability, affordability and access will European patients, healthcare systems, and broader society yield the benefits that vaccines can deliver.

	Opportunities to improve the policy environment for vaccine availability
 Availability	• Explore feasibility of greater flexibility in regulatory assessment in a non-emergency context and availability of alternative approval pathways for faster access to vaccine innovation • Ensure all countries implement mechanisms for early and continuous dialogue • Co-development of demand forecasting mechanisms to manage vaccine supply-demand to ensure market sustainability • Review NITAG composition and capacity and allocate necessary expertise and resources • Streamline NITAG evidence requirements and methodologies • Ensure no restrictions in population access beyond the marketing authorisation label, supporting a life-course approach to immunisation

	Opportunities to improve the policy environment for vaccine affordability
 Affordability	• Implement a dynamic approach to vaccine funding to adapt to unforeseen changes and shift towards a life-course approach • Ensure a forward-looking view for sustainable budget setting through multi-stakeholder collaboration, leveraging the ROI from vaccination

	Opportunities to improve the policy environment for vaccine access
 Access	• Prioritise strengthening vaccine manufacturing and supply chain resilience by developing guidelines on sustainable procurement best-practices that utilise multi-criteria decision analysis • Leverage mechanisms used for COVID-19 vaccine delivery to improve access points for life-course immunisation • Enable other healthcare workers, i.e., nurses/school-nurses, midwives and pharmacists, to prescribe and administer vaccines improve equity • Support European countries investments in developing infrastructure for RWE collection and immunisation monitoring across the life-course • Develop guidelines and campaigns at European-level to improve health literacy on the importance of vaccine prevention and dispel vaccine misconceptions

1. Introduction

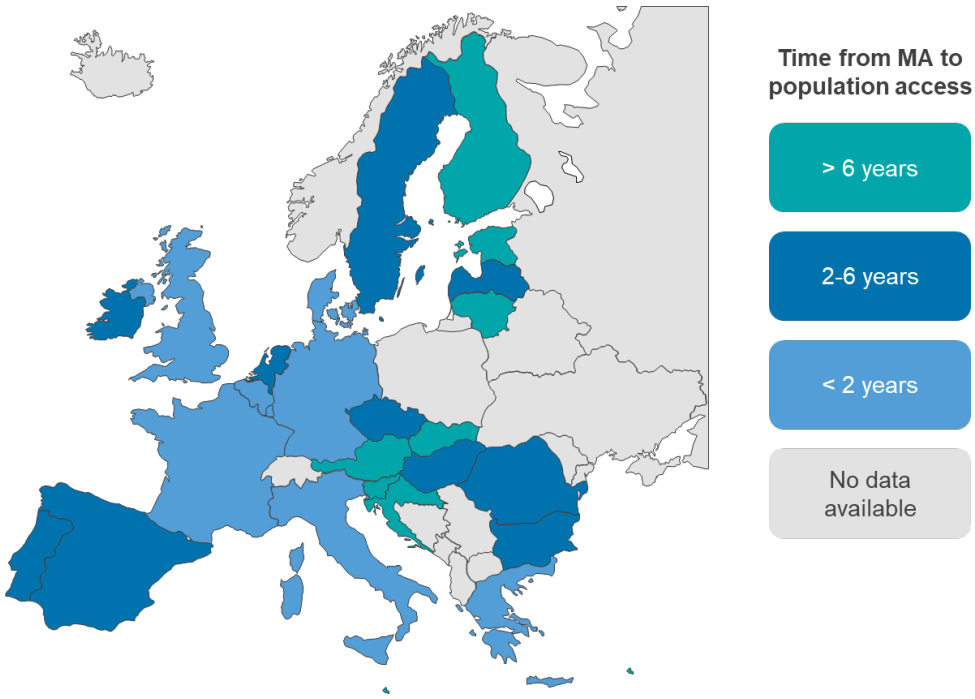
Charles River Associates ('CRA') was commissioned by Vaccines Europe ('VE') to develop an analysis of the policy issues affecting the availability, affordability, and access (AAA) of vaccines in Europe. The aim was to define the three 'A's" for routine vaccines, articulating differences between medicines and vaccines, collect evidence on the cause of each of the three 'A's for routine vaccines included in National Immunisation Programmes (NIPs), and how policy solutions could address these issues across the vaccine market access (VMA) pathway.

1.1. Background

Vaccination is a hugely successful and cost-effective health prevention tool that helps tackle public health threats.[5] Vaccines, unlike traditional medicines, provide benefits beyond individual disease protection by indirectly protecting the wider population upon mass coverage due to herd immunity effects. Currently, vaccines can protect people against over twenty diseases and there is a rich pipeline of new vaccines in development.[6] The latest review of VE members found that of the 103 vaccine candidates in the pipeline in August 2023,[7] 42% of the vaccine candidates aim to address diseases for which no vaccine has been registered until now. This underscores the continuous dedication to vaccine R&D for emerging health threats. 22 of the 100 investigated vaccinates are designated for routine immunisation in Europe. Over 80% of the candidates are tested exclusively in adults and older adults, reflecting the challenges ahead when it comes to a growing adult and older adult population. All these findings reflect the need for national immunisation programmes to adapt and recognise the importance of a life-course approach to vaccination. Only such an approach can ensure protection for individuals at all stages of life and strengthen public health efforts in the decades to come.

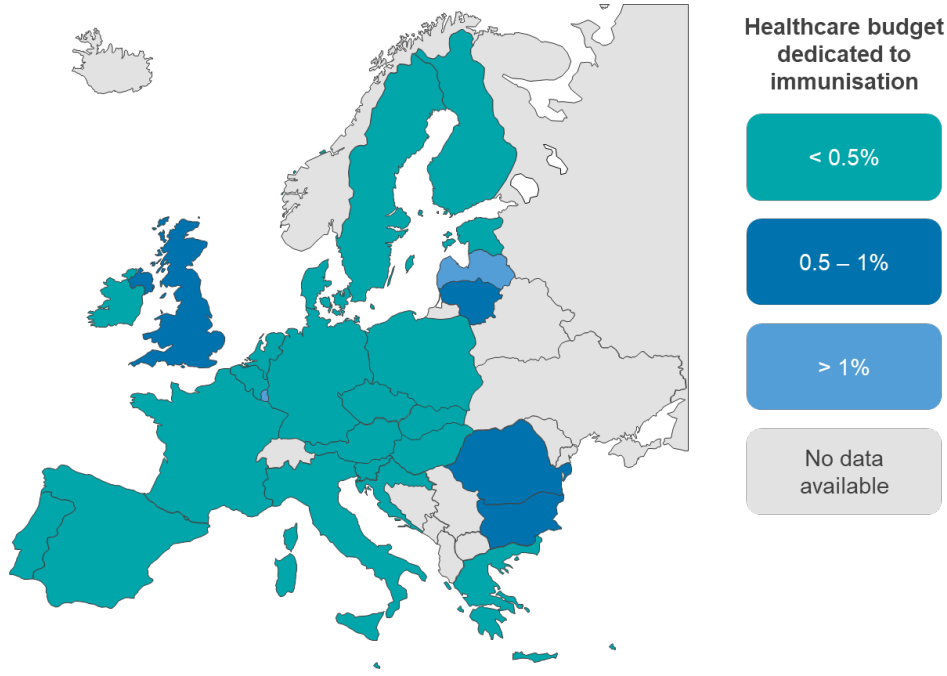
However, today we face significant differences across Europe in terms of the time it takes for a vaccine to become accessible (counted from the marketing authorisation to the moment when the public can physically receive the vaccination) due to delays in market authorisation or differing regulatory timelines. Some countries ensure access in less than 2 years, but for 30% of European countries, it can still take more than 6 years (see Figure 1).[4] Investment in vaccines also varies considerably from country to country, with only 5 European countries dedicating more than 0.5% of their healthcare budget to immunisation (see Figure 2).[3]

Figure 1: Time from marketing authorisation to population access across Europe



Source: Laigle et al. (2021)

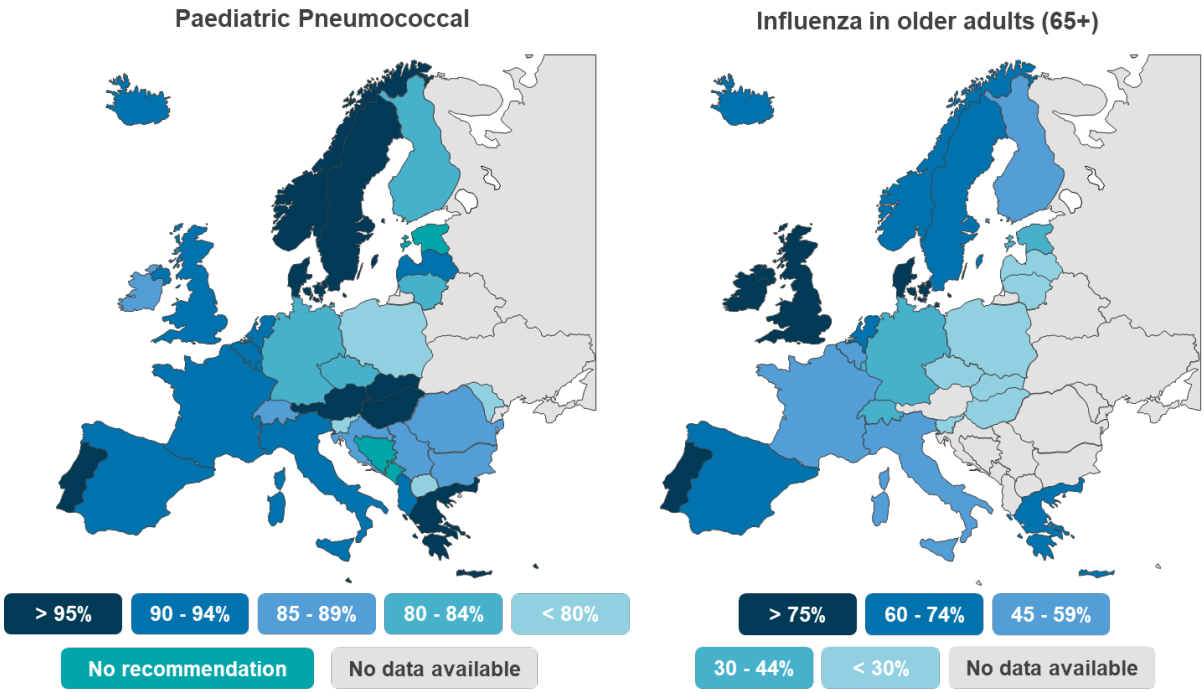
Figure 2: Percentage of national healthcare budget dedicated to immunisation across Europe



Source: Faivre et al (2021)

This variability in time to access and budget to support the implementation of NIPs can contribute to significant variation in vaccination coverage rates and vaccination schedules across Europe (see Figure 3).

Figure 3: Vaccination coverage rates for paediatric pneumococcal and influenza in older adults across Europe



Source: Pneumococcal Vaccination Atlas[8] and OECD[9]

Although there is some recognition that the policy issues affecting AAA for vaccines are different to that of medicines in Europe, it is still common for analyses to generalise barriers affecting vaccines to all medicinal products.[10] Indeed, the ongoing revision of the General Pharmaceutical Legislation could see legal provisions applied to vaccines with little regard for the different market dynamics of vaccines.[11] This is occurring alongside publications of global and European immunisation agendas with targets for the coming years, such as WHO's 'Immunisation Agenda 2030'.[12] Consequently, an analysis outlining the policy issues affecting AAA for vaccines is needed. This paper aims to define the three 'A's for vaccines, set out the underlying causes of the differences across Europe, and then provide policy solutions across the vaccine market access pathway.

1.2. Approach

The development of this paper involved conducting a comprehensive literature review and identifying and accessing a diverse range of sources from academic databases, industry reports, government publications, and international organisations. The review primarily focused on literature published within the last decade focused on European countries to capture ongoing debates and emerging trends. In total, 60 documents were analysed, examining "availability/NITAG", "positive recommendation/inclusion on NIP", "access/coverage", and "affordability". An internal workshop was then held with VE members to discuss the findings from the literature review and align on the definitions/goals of the three A's and the underlying policy issues affecting differences across Europe. Furthermore, 5 stakeholder interviews were conducted with a range of vaccine experts, including NITAG members, national payers, physicians, and academics across France, Italy, the Netherlands and Romania to validate the analysis. Technical officers for the WHO also provided additional insights.

This analysis intentionally concentrates on vaccines included in NIPs, as they are part of established and ongoing systematic immunisation initiatives implemented by national healthcare systems. Conversely, vaccines for emergency situations, vaccines that are typically paid for out-of-pocket, and therapeutic vaccines, were not considered within the scope of this analysis. Variation in the three 'A's

for these vaccines would have different underlying causes depending on the specific emergency need and therapeutic area.

It Is critical to acknowledge that COVID-19 vaccines so far have fallen into the category of emergency vaccines and are therefore not a central focus of this research. Specialised regulatory timelines and resource commitments are key limitations to explain why COVID-19-era vaccine policies are unlikely to be translated into the findings of this analysis.[13] Nonetheless, this narrative recognises that the rapid distribution of COVID-19 vaccines has potential lessons for the wider vaccine framework in Europe (see Figure 4). While this study will touch on some of these ripple effects, the primary aim will be to focus on the three 'A's for routine immunisation.

Figure 4: Comparison of the three 'A's for routine vaccines vs. COVID-19 vaccines

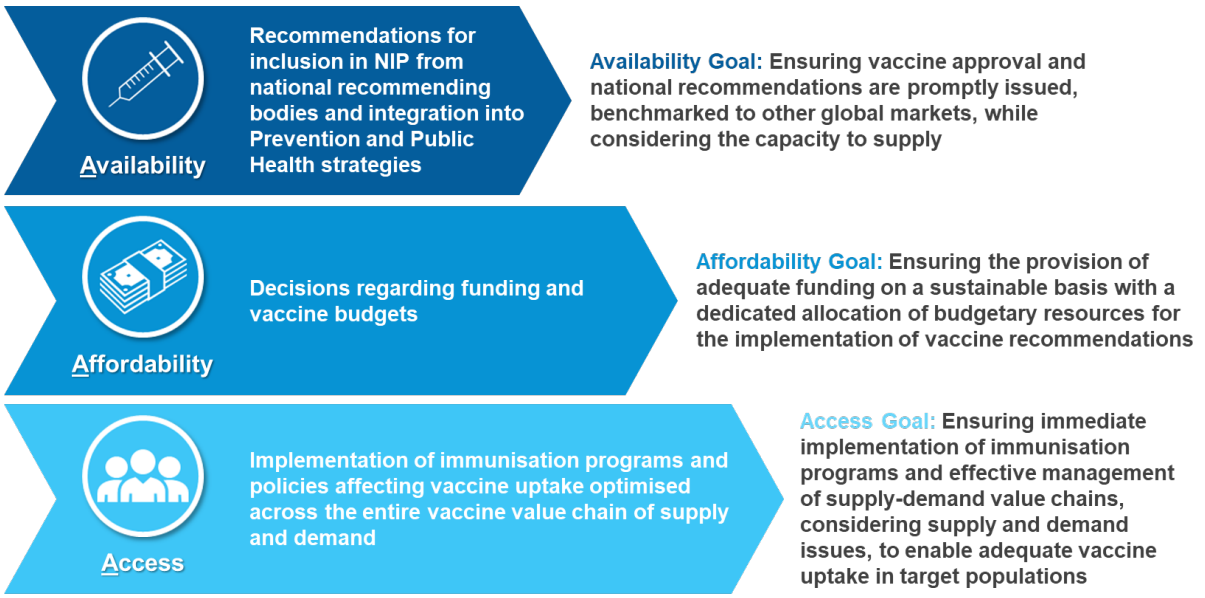
	Routine Vaccines	COVID-19 Vaccines	Lessons Learnt
Availability	• EMA has leveraged expedited pathways for only ~17% of non-COVID-19 vaccines • EMA median time to approval is 11.1 months • NITAG recommendation required for NIP inclusion	• EMA conditional marketing authorisation allowed for post-marketing data and rolling reviews • Median regulatory approval times was ~2 months • NITAGs forced to assess available evidence in parallel to national or regional regulators based on partially published or evolving data	The EMA and NITAGs have the capacity to dramatically improve approval times and expedite approval for emergency situations using innovative approaches such as joint assessments and regulatory agilities
Affordability	• Extremely small proportion of healthcare budgets (less than 0.5%) spent on vaccination	• COVID-19 vaccine access supported through use of emergency funds and supplementary budgets • Some countries allocated additional funds to national budgets	The use of excess emergency funds should not be standard for routine immunizations; however, the requirement for additional funds to support COVID-19 vaccine rollout implies inadequate budget allocation for new vaccines
Access	• Access points vary widely by vaccine and by country • Inconsistent financial and logistical burdens on patients and affordability across Europe	• Widespread expansion of access points across the life-course • Flexible guidelines on vaccine administration • Adoption of centralised e-health records	Simplification of the access pathway and the new infrastructure implemented for COVID-19 vaccine uptake could be leveraged to facilitate a more agile approach to broader access

2. How do we define availability, affordability, and access for vaccines?

The three A's—availability, affordability, and access—for vaccines have received more attention following the COVID-19 pandemic.[14] However, for the differences to be appropriately evaluated, it is useful to consider them as distinct, but interconnected policy areas. Following alignment at the VE workshop, it was agreed the three A's follow a cascade structure (see Figure 5), representing the sequential flow of the vaccine landscape. The cascade starts with "availability", this represents the initial step in the cascade regarding the inclusion in NIPs.[4] The vaccine inclusion on the NIP generally initiates discussions surrounding vaccine budgets and allocations within wider preventive health frameworks ("affordability"). Although not always sequential, these funding decisions then have a direct impact on the rollout of immunisation programmes and uptake within the population ("access").[15]

It is important to note that this conceptual framework exemplifies the interdependencies of the three A's through a cascade, rather than a strictly linear pathway. This is because the decisions in Europe can occur in parallel or independently within the cascade, overlapping across areas. For example, budgetary discussions may happen concurrently with NIP considerations, resulting in NIP restrictions due to budget constraints. Each of the three A's is associated with a clear goal that would support optimal vaccine uptake across Europe (see Figure 5). Drawing on the policy issues affecting the three A's, we propose policy solutions to ensure these goals can be achieved (see Section 4).

Figure 5. Agreed definitions and goals of AAA for vaccines



Source: Workshop with VE members with stakeholder interview input

3. What are the underlying causes of differences in AAA and is there evidence on the extent of the challenge?

3.1. Availability

For inclusion into NIPs, manufacturers must first be granted marketing authorisation by the EMA and then undergo individual national assessment across individual Member States.[4] Key steps at the national level include horizon scanning, early advice, NITAG assessment, and recommendations for consideration of vaccine into NIP.

Delays to marketing authorisation and the timeliness of regulatory revisions

The length of time taken to obtain marketing authorisation has a significant impact on vaccine availability as it represents the initial regulatory step. Any delays in this process can exacerbate the overall delay in population uptake. One of the key issues is the comparatively limited flexibility/ utilisation of expedited regulatory pathways for vaccines relative to other regions of the world. These pathways allow for vaccines to move through the regulatory process in a timely manner, contributing to faster population access to innovative vaccines. Since 2015, the EMA has leveraged expedited pathways for ~17% of non-COVID-19 vaccines.[16,17] This is in stark contrast to the FDA, which has utilised these mechanisms for >65% of vaccines.[17]

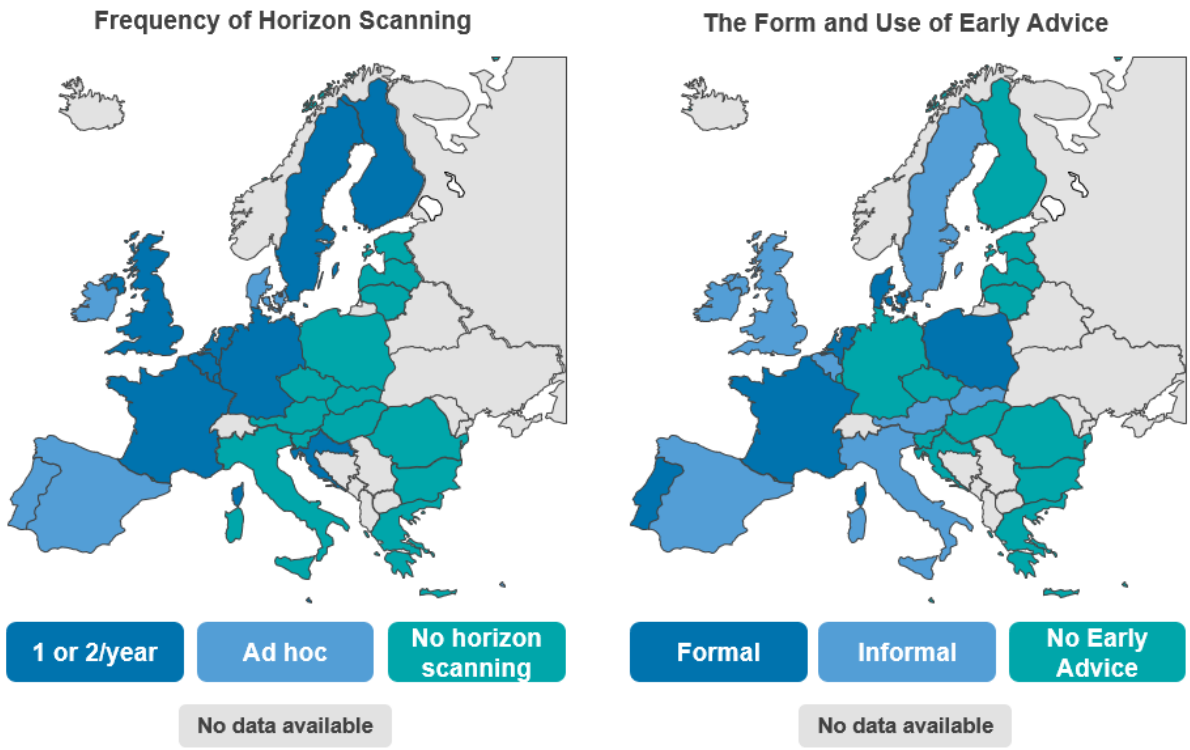
There also appears to be a missed opportunity in terms of utilising the learnings from the COVID-19 pandemic. During the pandemic, median regulatory approval times for COVID-19 vaccines were less than 2 months – this was achieved by leveraging various regulatory procedures such as rolling reviews and by prioritising workforce resources. Despite these successes, approval timelines post-pandemic have not shortened compared to before the pandemic, with the median time to approval still 11.1 months for the EMA, relative to 8.8 months for the FDA.[18] This suggests that Europe has not translated the learnings from the pandemic as well as other regions, which may be hindering population access to new vaccines and timely regulatory revisions. However, these are expected to change with the ongoing revision of the EU General Pharmaceutical Legislation.

Lack of early and continuous dialogue from recommending bodies with industry to better anticipate NITAG review timelines, HTA review procedures and demand planning for new and existing vaccines

Vaccine experts have acknowledged the importance of early advice and horizon scanning for acceleration of the NIP process. This is especially critical for the numerous pipeline candidate vaccines utilising new technology platforms. Early advice, whether provided formally or informally, offers manufacturers the opportunity to receive feedback on evidence requirements from NITAGs and HTA bodies. This facilitates early planning for assessors and ensures an efficient assessment that captures the wider benefits of vaccination (direct, indirect and societal). Simultaneously, it supports recommending bodies in numerous ways. Working in advance with NITAGs for example would assist in enabling earlier consideration and preparation of evidence required at the NITAG level, expediting access timelines.[13] Awareness of new and emerging vaccines in development allows recommending bodies to be better equipped to assess the feasibility of incorporating novel vaccines into immunisation strategies and plan for resource allocation, leading to better-informed decision-making. However, across 27 European countries, regular horizon scanning (conducted once or twice per year) is only performed in 15 countries, usually by the NITAG, Ministry of Health (MoH) or other institutions.[4] There are even fewer provisions for Early Advice. Formal Early Advice, involving the national competent authority with a separate, established process with clear criteria only features in 5 countries. Informal Early Advice features in 8 countries, and is usually provided verbally, in face-to-face meetings. For example, the German NIP process does not feature early advice, but manufacturers may present their data in meetings with the Robert Koch Institute (RKI).[4] Although the new EU Regulation on Health Technology Assessment (HTA) provide an opportunity for Europe-wide

horizon scanning, it is still unclear whether NITAGs will be actively involved in this process. Figure 6 provides an overview of the variability of horizon scanning and early advice activities across Europe.

Figure 6: Frequency of horizon scanning and form of early advice activities across Europe



Source: Laigle et al. (2021)

Misalignment of evidence requirements and evidence value due to varying healthcare system processes

NITAGs are established expert panels appointed by national health authorities to assess vaccines and provide recommendations and guidance on immunisation policies. In addition to assessing the vaccines themselves, NITAGs also inform the overall immunisation strategy, including the timing and scheduling of doses, the target population, and the necessary infrastructure required to ensure widespread adoption of vaccine programmes, such as training of healthcare personnel and monitoring systems. NITAG assessments typically see vaccine safety, efficacy, and burden of disease as important considerations for NIP recommendations, but in some countries, other factors play a more dominant role than others. In countries like the Netherlands and Finland, which have centralised systems and government-funded vaccination programmes and procurement, health-economic evaluations hold significant weight compared to countries like Germany where vaccine reimbursement follows physician recommendations.[2] Additionally, NITAG assessments may also vary in their involvement of broader stakeholders such as national public health organisations, national health authorities, and/or infectious disease groups.[19] While such diversified stakeholder engagement is favourable to inform a holistic NITAG assessment, it may also result in discrepancies in evidence assessors and requirements, particularly if stakeholders are recruited more informally on an ad-hoc basis. This broad inconsistency potentially causes issues for manufacturers, having to tailor their evidence packages to secure a positive NITAG recommendation, which may have profound implications on delays or even disparate decisions regarding vaccine inclusions. Mitigating the impact of different evidence requirements is critical to achieving an equitable immunisation landscape.

However, a more pressing concern is the inadequate inclusion of vaccine-specific factors such as ethical considerations and the concept of herd immunity in the assessment processes.[20] In fourteen

European countries that conduct HTA for vaccines, only four of them utilise a vaccine-specific decision-analysis framework; therefore, vaccines are still largely assessed similarly to medicines.[21] While countries may not be lacking in vaccine expertise per se, there is a lack of time and resources dedicated to NITAG work and task management.[13] The omission of vaccine-specific evidence may hinder a fully comprehensive assessment. Certain stakeholders advocate for advancing knowledge exchange across Europe and establishing a shared evidence base for vaccines as the logical progression for member states. While acknowledging the significant advantages of streamlining decision-making processes, there are notable queries and concerns regarding the need for assessors and assessments to be vaccine-centric and tailored specifically for assessing vaccines, rather than imposing 'one size fits all' methodologies used for medicines. As Europe shifts to a centralised assessment system through the EU HTA framework, the eventual sharing of evidence for vaccines is anticipated. However, the implementation of vaccines' specificities in the new framework, along with the methods and extent of their influence on decision-making and integration into national immunisation plans, remains ambiguous. These prominent questions must be answered before implementing any type of joint assessment.

Heterogenous national assessment systems with limited life-course vaccine prioritisation and lack of transparency with vaccine manufacturers and the public

The key stakeholders involved in the NIP process vary widely across Europe. Established Health Technology Assessment Bodies (HTABs) routinely assess medicines, providing a relatively standardised approach. However, when it comes to the assessment of vaccines, the national processes within Europe exhibit a higher degree of inconsistency and unpredictability.

The HTAB recommendation follows or is made in parallel to the NITAG Recommendation, in 12 of 27 European countries.[4] Looking at NITAGs, their composition, decision-making processes, and ways of working also vary significantly. A study examining 22 European NITAGs revealed that only 16 countries included specialists in vaccinology and immunology (see Table 1).[2] This is quite concerning as recommending bodies are required to cover the evaluation of all vaccination types across therapeutic areas and target populations; these comprehensive evaluations require specialised vaccination expert panels.[22] The ideal NITAG committee should prioritise clinical specialists as the clinical perspective is critical in understanding the vaccines' value.[13] The other expert groups that are consulted are predominantly paediatricians. This composition raises concerns as paediatricians may not provide comprehensive advice on adult vaccination. Additionally, there was a notable absence of diverse experts such as health economists and sociologists. Diverse experts are needed to provide valuable insights into the comprehensive value of vaccination, for example, health economists could inform the trade-offs between costs and benefits of a new intervention.

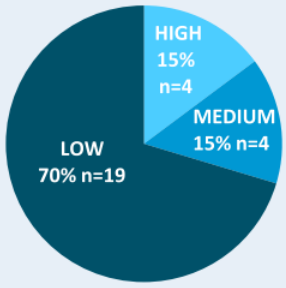
Table 1: Professional expertise represented among NITAG members in 22 European countries

Professional Field	Countries	Proportion of representation across 22 European countries (%)
Clinical medicine	22	100
Epidemiology	21	96
Paediatrics	20	91
Public health	18	82
Microbiology (incl. Virology)	17	77
Immunology	16	73
Vaccinology	16	73
Health economics	5	23
General practice	5	23
Regulators	5	23
Ministry of Health	2	9
Social sciences	2	9

Source: Nohynek et al. (2013)

The frameworks for vaccine assessment within NITAGs and HTABs exhibit significant variability across countries, and only a limited number of countries publish their rationale for negative or positive decisions regarding vaccine inclusion in NIPs.[23] Established methodologies can improve speed of access but NITAGs often face issues with evidence and time.[13] Unsurprisingly, transparency levels of NITAGs and HTABs for vaccine assessment were rated low by vaccine experts (defined as one transparency criterion being met) in 70% of 27 European countries (see Figure 7).[4]

Figure 7: Transparency of NITAG decision-making across 27 European countries

NITAG (n=27) transparency criterion	n	Transparency level
Formal decision-analysis framework	7	
GRADE or a similar tool used for the quality of evidence and risk of bias assessment	2	
Recommendations publicly available	16	
Rationale for the decision publicly available	14	

Source: Laigle et al. (2021)

It seems reasonable to conclude that limited transparency in the vaccine assessment frameworks of NITAGs and HTABs presents a significant hurdle to ensuring equitable access to vaccines. Without understanding the rationale for previous negative or positive decisions, manufacturers are unable to incorporate this feedback to increase the likelihood of positive decisions for future vaccines. Furthermore, NITAG experts highlighted that there is a need to provide NITAG appraisal information to the public to enhance overall information about vaccines and increase trust in recommending

bodies.[24] This issue becomes even more pressing as an increasing number of unique and diverse vaccines emerge from the pipeline to address novel disease areas.

Restrictions in the recommended target population due to the influence of budgetary concerns rather than public health considerations

NITAGs can include members beyond clinical and public health experts, such as the Ministry of Health (see Table 1).[2] The inclusion of diverse experts in NITAG panels can allow for a broader perspective on vaccination programmes, enriching the decision-making process. However, the central challenge lies in maintaining the scientific and public health-backed focus of NITAGs amidst the informal and formal influence of external factors, such as budget considerations. Striking the right balance between diverse expertise and scientific rigour is essential to ensure robust and unbiased recommendations for vaccination programmes. Thus, it is important that the views of different stakeholders are given appropriate weight.

This concern revolves around the criteria and processes used for assessment, most of which are often not disclosed to the public.[24] While diversity in representation is valuable, the influence of external factors, whether from formal NITAG panel members or external sources like policymakers and the government, should not compromise the scientific integrity of NITAG decisions. An example illustrating this concern occurred in Romania, where the inclusion of paediatric pneumococcal vaccines should have been recommended in the NIP in 2013 but was delayed due to funding concerns to support the effective introduction of the vaccine. Consequently, the vaccine was not recommended until 2017, limiting uptake and vaccination coverage.[25] As new vaccines are developed, ensuring inclusive guidelines that facilitate vaccine schedule integration and high uptake becomes increasingly important.[26]

3.2. Affordability

The level of funding for immunisation programmes should reflect the evolving epidemiology of vaccine-preventable diseases coupled with changing socio-economic and demographic needs across Europe, which on the other hand can be influenced by the inclusion of a new vaccine to the market. Vaccination affordability extends to a broader budget allocation covering the general population, provided they meet the vaccine's eligibility profile and target age range and are used across the patient's life-course. This is unlike the decision regarding the affordability of medicines, which pertains to whether the benefits of a medicine to specific patients or groups outweigh its costs. Immunisation programmes mostly cater to healthy individuals (not carriers of a disease the vaccine aims to prevent). The relevant populations for vaccines are much broader than medicines as the value of these programmes often hinges on achieving sufficient coverage across the entire population to obtain potential savings from preventing illnesses, increasing budget impact. Consequently, vaccination affordability encompasses not only the price of the vaccine itself but also the financial capacity to support the implementation of a new vaccination programme or the expansion of an existing programme to reach a new target population, that spans a wide and diverse population across the entire life course. These broader costs could include, but are not limited to, distribution, administration, cold chain infrastructure, medical supplies, training, outreach campaigns, community engagement, data collection as well as assessment of the impact of vaccinations. Affordability decisions need to be forward looking considering a holistic perspective of the population-level benefits and broader costs throughout the implementation of vaccine use.

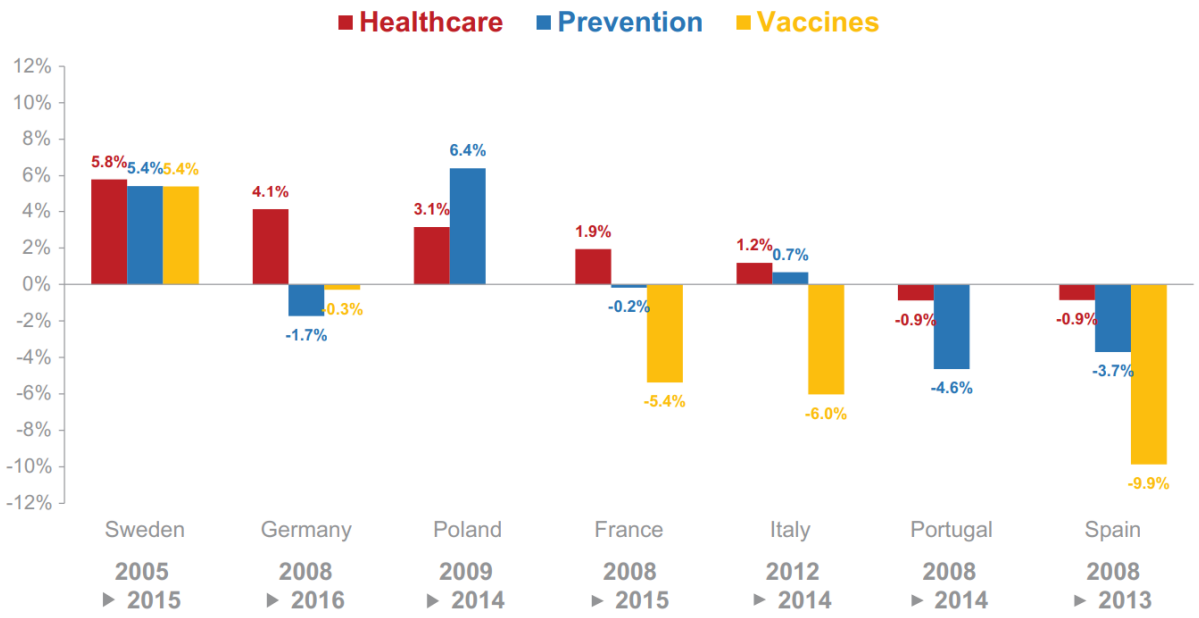
Insufficient budget allocated for effective implementation of NIPs to fulfil the needs of target populations

Immunisation, acknowledged as a well-established, cost-effective, and life-saving health intervention, is generally appreciated for its role in disease prevention, though this value may vary in different contexts. However, there is growing concern about the relatively low level of investment in vaccination programmes within Europe, and in some instances, this funding is on a declining trajectory.[27]

Ensuring vaccinations are used across the target population is critically important as they not only help reduce the risk of disease transmission within specific groups who are vaccinated, but also contribute to the attainment of herd immunity in the wider population. Thus, vaccination initiatives play a multifaceted role in protecting individuals and communities. NIPs offset their costs multiple times through benefits to individuals, the healthcare system, and wider society. Adult vaccination programmes can return up to 19 times their initial investment when the full spectrum of economic and societal benefits is valued.[28] The 19x return is equivalent to up to USD 4,637 in net monetary benefits to society per individual full vaccination course. However, the societal value of vaccinations is often invisible and can be overlooked.

Prior to the pandemic, there was a noticeable decline in vaccination funding, which raises concerns. For example, a study of 7 European countries found that vaccine spending per capita has decreased in most countries between 2005 and 2018 and Sweden was the only country to have increased its investment in immunisation over the last decade (see Figure 8).[32] However, more recent data also shows an increase in vaccine expenditure in Italy, with the per capita expenditure on vaccines more than doubling from 2014 to 2021.[29] Indeed, less than 0.5% of healthcare budget is allocated to vaccinations in 77% of European countries, significantly less than the 20% allocated to medicines.[3]

Figure 8: Evolution of healthcare, prevention and vaccine expenditure per capita



Notes: Estimates are from national sources and the % figures are the CGRs over the corresponding time period.

Source: Ethgen et al. (2018)

Furthermore, these budgets are set on a short time horizon and fail to consider the long-term horizon for vaccine development and reaping the benefits of long-term vaccine protection.[13] In practice, adult immunisation programmes are shown to return up to 19 times their initial investment to society when their positive externalities are monetised.[28] However, these long-term benefits are often outside the scope of political agendas that are focused instead on goals aligned with electoral cycles.[22] There is a clear discrepancy between the acknowledged importance of vaccination and the allocation of

budgets, given that allocations are quite small compared to medicines.[3] Despite established medical recommendations for positive inclusion in NIPs, budget holders tend to be much more conservative with endorsing vaccines for NIP inclusion as there are concerns about budget impact. Furthermore, the risk of poor adherence due to vaccine hesitancy can result in insufficient herd immunity, decreasing the return on investment from a budget perspective.[19] As new vaccines become available, increased allocation of resources for broader value assessment and high adherence will be critical to ensure public access to these life-saving tools.

Amid the pandemic, novel funding mechanisms were introduced to support large-scale COVID-19 vaccination efforts. However, it is critical to recognise that altering funding models for vaccinations is a complex and challenging endeavour. And hence, the impact of the pandemic makes it difficult to consider recent trends in immunisation funding.

Inability of budgets to have the flexibility to adapt to changing public health needs and ongoing vaccine innovation

The heterogeneity in vaccine approval processes in Europe is also reflected in the varied approaches taken by countries when determining and updating their budgets for vaccinations. Setting such vaccination budgets should account for both current public health needs and innovations in vaccine development to best meet population needs. While some countries stand out for their dynamic budgets and proactive strategies, many others lack a comprehensive approach.[30] A review of the budget-setting process across select European countries indicated that adequate and dynamic country vaccine budgets, like in Finland, or flexible vaccine expenditures like in Germany, would greatly help the timely availability of public funding for vaccines, both existing and innovative, and would strengthen the vaccines supply security in Europe. By allowing budget supplementation as needed based on emerging priorities and allocating funds for both vaccine costs and service delivery, countries such as England and Finland adapt much more swiftly to public health needs, cross-border health threats and changing vaccine developments, compared to their European counterparts.[39] This flexibility is critical to future NIP design and implementation, as well as other aspects of public health.

Lack of alignment between national and regional decision-makers on public health priorities and budget allocation

While most countries establish healthcare budgets at a national level, some countries also involve regional-level decision-making. The presence of national and regional approvals, along with the complexity of multiple layers of budget allocation processes, has led to documented delays for medicines in Europe.[31] This has also been observed for vaccines. The variation in decision-making authority, clarity, and the need for regional consensus across countries significantly impacts the budget allocation for vaccines.

Regional interests can diverge from national interests as they focus on the specific needs of their populations. Consequently, regional budget allocation can potentially impose restrictions and delay population access to vaccines, despite national interest. Different countries have adopted different approaches to this issue. For example, Italy requires unanimous regional consensus prior to granting a final positive national-level vaccine decision and all vaccines recommended in the NIP are required to be reimbursed in all regions as they are included in the National Essential Level of Assistance.[4] In contrast, regional health agencies in France have limited autonomy to divert or amend vaccine funding based on decisions made at the national level.[39] In other countries, regional authorities can introduce additional considerations that may influence access to vaccinations, potentially leading to variations between regional and national coverage.

3.3. Access

The underlying differences in access across member states stem from the variations in the effectiveness of implementing national immunisation programmes. Efficient management of supply and demand dynamics is critical in addressing these issues and enhancing overall vaccine access;

there is often a gap between the demand side and the supply side, where demand for new vaccines from policymakers and populations does not take into account supply schedules and manufacturing capacity or there is insufficient demand.[12] These programmes rely on supporting enablers that aim to achieve optimal uptake of vaccines in target populations. Various issues impact the sequence of steps at the national level that lead to uptake: procurement, access points, administration, equity, monitoring, and education.

Procurement practices that reduce market attractiveness and limit supply adaptability to evolution of population needs that do not account for overall vaccine manufacturing challenges

In the majority of European countries, vaccines are procured via competitive bidding processes such as tenders. Traditional tenders often take a 'winner-takes-all approach' where a single supplier is awarded the entire contract for vaccine procurement based on specific criteria. This is often based on the supplier offering the lowest price. Some tenders can take on more flexible forms that allow for multiple suppliers and additional consideration of factors beyond price such as quality, delivery reliability, and responsiveness to public health needs.

While traditional price-based vaccination procurement can bring short-term financial savings, they can be damaging to the sustainability of immunisation programmes in the longer term because they make the market less attractive. This is especially challenging when vaccine target populations are expanded to new subpopulations and demand fluctuates.[13] When the low level of prices means that suppliers cannot make a commercial return on the markets, they may choose to exit the market altogether, resulting in very few suppliers. Not only does this increase the potential for supply interruptions but also, as competition is reduced, this could lead to lower levels of investment in the market or even higher prices.[22] Since Spain has implemented price-based tenders for vaccines, it has experienced problems in attracting bids, particularly for diphtheria, MMR, tetanus, pertussis, pneumococcus, typhoid fever, rabies, and yellow fever vaccines due to the lower market attractiveness to companies.[32] In response, the government increased the MMR price in 2014 as an incentive to suppliers to continue supplying the Spanish market. GAVI, which purchases vaccines for many low and middle-income countries, has recognised the negative externalities stemming from price-based market-shaping activities, and has sought to monitor and since revised its procurement strategy.[33] Also, following concerns of consolidation of the marketplace the United States changed their vaccine tender frameworks to facilitate long-term competition in the vaccine market by moving away from price-based tenders.[34]

Furthermore, the challenge in vaccine procurement extends beyond the choice of tender model. Procurement practices and procedures can struggle to account for the complexities of vaccine manufacturing, which are both lengthy and complex. These challenges can affect vaccine availability and timelines, particularly when addressing evolving epidemiological patterns and emerging public health demands. For example, in 2008 the Ministry of Public Health in Romania purchased a volume of influenza vaccines that was grossly inadequate for the population. Due to the tender process for vaccine procurement, the tender process was re-run and manufacturers struggled to manufacture the volume needed in a timely manner. This resulted in a period where the market had an insufficient quantity of influenza vaccines.[35] In Germany, several federal states awarded a sole supplier the responsibility of supplying influenza vaccines for the year 2012. Due to identified impurities, this supplier was unable to deliver the contracted one million doses. The tender framework at the time only solicited one supplier and no other influenza suppliers had produced or stocked excess doses. This presented a challenging situation in which the states could not purchase from another producer and had to solicit vaccines from other federal states.[44] This issue has been addressed by moving away from reliance on a single supplier tenders.

The reliance on traditional price-based tenders as the primary procurement method can undermine the stability of vaccine supply, ultimately jeopardising public health. While tenders can vary in their approach, Europe should encourage more sustainable procurement practices and procedures to

address the complex nature of vaccine manufacturing and evolving public health needs. Vaccines transcend mere commodities, playing a pivotal role in public health. In recognition, there have been efforts by bodies such as the WHO to ensure sustainable supply management.[12] Similarly, the European Joint Action on Vaccination (EU-JAV) has also prioritised strengthening vaccine supply and preparedness in Europe as one of their key workstreams with recommendations for improved data sharing on vaccine supply/demand to prevent vaccine shortages.[36] Moving forward, a comprehensive approach to procurement for countries that considers price, quality, flexibility, and manufacturing needs is needed to better serve the long-term goals of immunisation programmes.

Limited expansion of vaccination access points for effective implementation of life-course immunisation to support equitable access

Health system barriers to vaccination delivery, such as distances to access points or staffing resources can limit equitable access across the target population. Achieving high levels of immunity in the population through vaccination requires equitable access to vaccination centres and services. Equitable access points are determined by the location of immunisation delivery and the availability of vaccination opportunities throughout the life-course. Vaccines can be delivered outside of health clinics, for instance in schools, workplaces, pharmacies, community centres, hospitals, maternity services or at home. For example, many countries have offered school-based vaccination against HPV, which increased rates of vaccination initiation/completion and lowered inequalities based on socioeconomic factors.[37] Such initiatives are further promoted under the European Commission's proposal for a Council Recommendation on vaccine-preventable cancers.[38]

Differences in guidelines and involvement of HCPs in vaccine administration

In some European countries, only licensed family doctors can vaccinate. This may limit the flexibility of a service and add unnecessary costs.[39] Enabling other healthcare workers such as nurses, midwives, school nurses and pharmacists to vaccinate may help increase equity. In Switzerland for example, school nurses play a vital role in administering vaccines to students; it was shown that cantons with school-based delivery of HPV vaccination had a greater VCR compared to those without.[40] Similarly, positive experiences with COVID-19 vaccine administration in community pharmacies prompted countries like Belgium to expand pharmacy access points, exemplified by a new bill approved in October 2023 for influenza vaccinations.[41] However, prescription requirements can still lead to limitations in coverage. Understanding the root causes of pockets of unvaccinated or under-vaccinated groups can guide more targeted and tailored interventions to increase uptake.

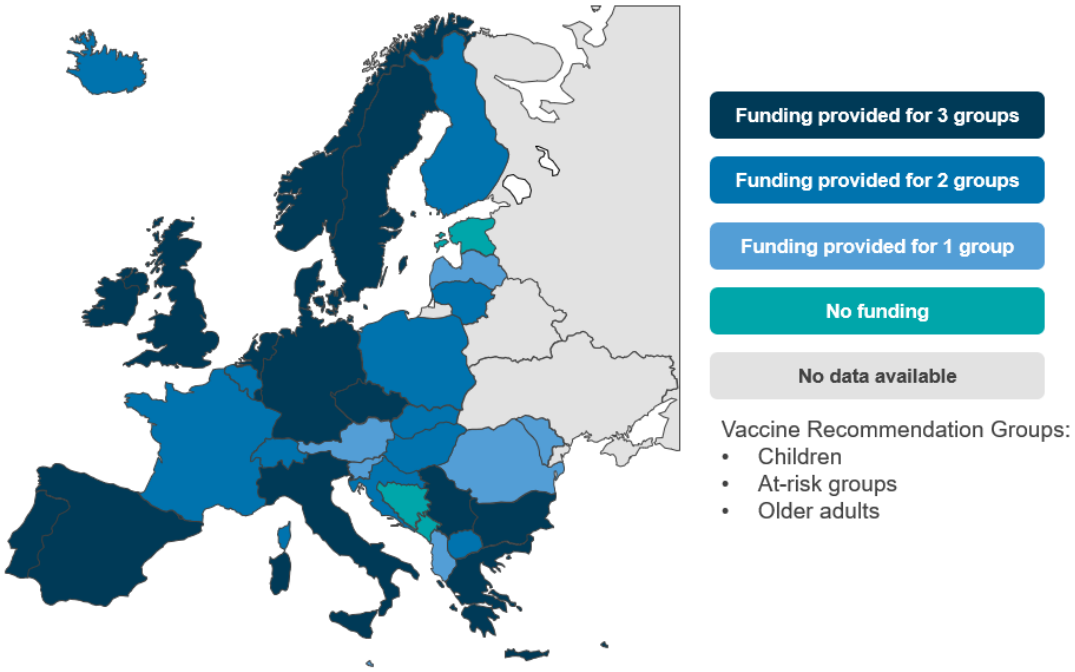
More than two-thirds of Europeans can access a pharmacy within five minutes, often this means they can consult a community pharmacist without an appointment.[42] However, there are still only 12 countries where pharmacists can vaccinate for COVID-19 and influenza and only 6 countries offer administration of other vaccines.[41] Numbers from Ireland have shown that since pharmacists first started vaccinating in 2011, flu vaccine deliveries through the National Immunisation Office (NIO) have increased overall by 48% and, within that, deliveries to general practitioners increased by almost 23%. Expanding administration to pharmacists can have a significant impact on increasing vaccine uptake. There are other established examples across Europe where pharmacists are having a hands-on role in administering vaccines, such as in Denmark, France, Portugal, and Spain.[44,43] However, in many countries that exhibit lower vaccination coverage rates, pharmacists are not allowed to take on this role. To increase vaccine coverage and help tackle vaccine hesitancy, it is crucial to make better use of pharmacist-delivered vaccination services as an integral part of NIPs.

Policies affecting equity and individual patient affordability, e.g., co-payments

Individual patient affordability is another barrier that prevents patients from maintaining all their routine immunisations. This is particularly pronounced when we consider life-course immunisation. In Poland, for example, there are eight vaccines on the national immunisation schedule that are recommended throughout the life-course but not publicly funded.[3] There are significant funding differences across life-course populations eligible for pneumococcal vaccinations: paediatrics, clinical at-risk groups, and

older adults (see Figure 9).[44] These funding differences are not consistent with national NIP recommendations.[45] A lack of core funding for pneumococcal vaccination programmes could explain why uptake is lower in some populations across countries, especially if patients are obliged to cover costs. This could exacerbate socioeconomic differences such as rural and urban divides that account for lower uptake within countries.

Figure 9: Funding for pneumococcal vaccination programmes across Europe



Source: Coalition for Life-Course Immunisation

Lack of infrastructure to collect, monitor and evaluate RWE to support appropriate vaccine uptake in target populations, limiting VCR

The availability of accurate and recent data is integral for convincing policymakers and guiding updated improvements in vaccination efforts. Across Europe, there is significant heterogeneity in vaccine monitoring policies, coupled with limited guidance from the European level.[46] This is particularly evident when comparing across the life-course. For example, 98% of countries officially reported on childhood pneumococcal vaccination, while only 26% collected some form of data for people from clinical risk groups and older adults.[44] Many countries do not have the systems in place to collect, monitor, and evaluate real-world evidence and therefore cannot supply their policymakers with timely data that accurately reflects the needs of their population.[12] While the European Commission has engaged in improving the healthcare infrastructure with the proposal of the European Health Data Space (EHDS) and developing guidelines for immunisation information systems (IIS), there are still issues that remain when implementing such initiatives in practice.[47] In Romania for example, there are current issues with missing vaccine registries for patients receiving vaccinations in pharmacies, causing significant challenges for shaping the vaccine schedule.[27] This data deficiency ultimately affects vaccine access as it means it is difficult to accurately identify and quantify under-vaccinated populations and assess the actual impact of vaccination programmes. This data is critical to making informed decisions about resource allocation, targeted interventions, and programme adjustments for current and future vaccination programmes. When such data is unavailable, outdated, or of poor quality, these decisions are made without accurate insights, leading to suboptimal vaccination strategies. Numerous studies examining Europe's vaccine market access often cite the lack of data or the ability to access this data as a key limitation in their analysis. There is

a need for centralised recommendation from governing bodies to ensure robust systems are in place.[13]

Lack of comprehensive education for HCPs and the public, increasing vaccine hesitancy and hindering acceptance of new vaccines

The increased availability of online resources for health information has contributed to increased vaccine hesitancy and the spread of misinformation.[48] The threat of misinformation has resulted in vaccine hesitancy being identified as 1 of the 10 greatest threats to Global Health.[49] Studies show that vaccine acceptance has fallen in many European countries due to anti-vax social media movements and misinformation campaigns.[50] While hesitancy is pertinent for new vaccines, there is also a steady decrease in vaccination rates for established childhood vaccines and scattered epidemics of preventable illnesses such as measles.[27] With countries experiencing outbreaks of measles and other vaccine-preventable diseases, many have been forced to adopt new approaches to increase vaccination coverage.[51] For example, the Italian Ministry of Health implemented the Lorenzin decree in 2017, mandating ten childhood vaccinations (polio, diphtheria, tetanus, pertussis, haemophilus B, hepatitis B, measles, mumps, rubella, varicella) to attend educational services and avoid financial sanctions.[13,52] Vaccine hesitancy continues to be an issue post-COVID-19 pandemic, with a recent survey finding that some countries, such as Poland, now have notably higher hesitancy levels than global averages[53]. Across Europe, there is also an added issue of a widening 'vaccine confidence gap' between the older (above 65-year-olds) and younger (18–34-year-olds) generations, with the younger groups becoming increasingly less confident between 2018 to 2022.[54] This issue differentiates vaccines from therapeutics; while therapy hesitancy may only affect the individual, vaccine hesitancy can have wide-reaching consequences on entire populations.

Currently, there are insufficient resources dedicated to comprehensive educational initiatives to combat vaccine hesitancy. In particular, the main barriers against such initiatives are organisational limits, shortage of dedicated personnel and insufficient funding.[55] Beyond just vaccine hesitancy, HCPs also need to be made aware of new vaccines and there is decreasing medical advocacy for new vaccine solutions from a medical perspective.[22] However, educating HCPs must be implemented in a manner that enables staff to effectively manage new services, and not be overburdened with additional responsibilities. The WHO SAGE working group on vaccine hesitancy found that the provision of communication training for HCPs had positive effects on vaccine uptake, while information-based training generally had poor effect.[56] Initiatives aimed at improving knowledge, attitudes, and confidence for HCPs and awareness for the public such as PROTECT-EUROPE for HPV vaccinations, are critical to increase confidence in vaccines and achieve optimal immunisation rates.

4. Policy Opportunities

Understanding the root cause of the three 'A's across Europe is useful for considering potential policy solutions. Based on the key findings and supporting evidence identified throughout the research, we identified a number of opportunities to improve the policy environment to address the underlying causes of differences across the three 'A's. Given the multifactorial root causes, there is a need for a multi-stakeholder dialogue on how to improve the policy environment. Only by addressing the underlying causes of variation in availability, affordability and access will European patients, healthcare systems, and broader society yield the benefits that vaccines can deliver.

4.1. Availability

The goal for availability is ensuring vaccine approval and national recommendations are promptly issued and benchmarked to other global markets while considering the capacity to supply. VE advocates for expanded eligibility of expedited pathways and parallel review under the ongoing EU General Pharmaceutical Legislation revisions. Partnerships are ongoing to support the development and implementation of vaccine-specific value assessment methodologies, ensuring these are recognised as part of the EU HTA Regulation. Table 2 sets out opportunities to improve the policy environment for vaccine availability.

Table 2: Opportunities to improve the policy environment for vaccine availability

Underlying causes of differences in affordability	Opportunities to improve the policy environment
• **Delays to marketing authorisation and the timeliness of regulatory revisions** • **Lack of early and continuous dialogue from recommending bodies with industry to better anticipate NITAG review timelines, HTA review procedures and demand planning for new and existing vaccines** • **Misalignment of evidence requirements and evidence value due to varying healthcare system processes** • **Heterogenous national assessment systems with limited life-course vaccine prioritisation and lack of transparency with vaccine manufacturers and the public** • **Restrictions in the recommended target population due to the influence of budgetary concerns rather than public health considerations**	✓ Explore the feasibility of greater flexibility in regulatory assessment in a non-emergency context and the availability of alternative approval pathways for faster access to vaccine innovation ✓ Ensure all countries implement mechanisms for early and continuous scientific dialogue ✓ Co-development of demand forecasting mechanisms to manage vaccine supply-demand to ensure market sustainability ✓ Review NITAG composition and capacity and allocate necessary expertise and resources ✓ Streamline NITAG evidence requirements and methodologies ✓ Ensure no restrictions in population access beyond the marketing authorisation label, supporting a life-course approach to immunisation

4.2. Affordability

The goal for affordability is ensuring the provision of adequate funding on a sustainable basis with a dedicated allocation of budgetary resources for the implementation of vaccine recommendations. There is an increasing body of evidence on the socio-economic benefits of vaccines and the return on investment (ROI) for society. Table 3 sets out opportunities to improve the policy environment for vaccine affordability.

Table 3: Opportunities to improve the policy environment for vaccine affordability

Underlying causes of differences in affordability	Opportunities to improve the policy environment
• **Insufficient budget allocated for effective implementation of NIPs to fulfil the needs of target populations** • **Inability of budgets to have the flexibility to adapt to the changing public health needs and ongoing vaccine innovation** • **Lack of alignment between national and regional decision-makers on public health priorities and budget allocation**	✓ Implement a dynamic approach to vaccine funding to adapt to unforeseen changes and shift towards a life-course approach ✓ Ensure a forward-looking view for sustainable budget setting through multi-stakeholder collaboration, leveraging the ROI from vaccination

4.3. Access

The goal for access is ensuring immediate implementation of immunisation programs and effective management of supply-demand value chains, considering supply and demand issues, to enable adequate vaccine uptake in target populations. Industry continues to collaborate with different stakeholders to help improve access challenges for new and existing vaccines. Table 4 sets out opportunities to improve the policy environment for vaccine affordability.

Table 4: Opportunities to improve the policy environment for vaccine access

Underlying causes of differences in access	Opportunities to improve the policy environment
• **Procurement practices that reduce market attractiveness and limit supply adaptability to evolution of population needs that do not account for overall vaccine manufacturing challenges** • **Limited expansion of vaccination access points for effective implementation of life-course immunisation to support equitable access** • **Differences in guidelines and involvement of HCPs in vaccine administration** • **Policies affecting equity and individual patient affordability, e.g., co-payments** • **Lack of infrastructure to collect, monitor and evaluate RWE to support appropriate vaccine uptake in target populations, limiting VCR** • **Lack of comprehensive education for HCPs and the public, increasing vaccine hesitancy and hindering acceptance of new vaccines**	✓ Prioritise strengthening vaccine manufacturing and supply chain resilience by developing guidelines on sustainable procurement best-practices that utilise multi-criteria decision analysis ✓ Leverage mechanisms used for COVID-19 vaccine delivery to improve access points for life-course immunisation ✓ Enable other healthcare workers, i.e., nurses/school nurses, midwives and pharmacists, to prescribe and administer vaccines to improve equity ✓ Support European countries' investments in developing infrastructure for RWE collection and immunisation monitoring across the life-course ✓ Develop guidelines and campaigns at European-level to improve health literacy on the importance of vaccine prevention and dispel vaccine misconceptions

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