Enhancing Pathways for Vaccine Assessments and National Decision-Making

Vaccines Europe Policy Paper | November 2022

SUMMARY

Vaccine assessment and decision-making pathways are a key component of immunisation systems. They determine which vaccines are included in National Immunisation Programmes and contribute to the resilience of health systems. Enhancing the design and functioning of these pathways can improve the timeliness of population access to vaccines, support the shift towards life course immunisation, and strengthen efforts to improve vaccine confidence – thereby strengthening immunisation systems as a whole.

A unique research project by Vaccines Europe[1] has highlighted a range of ways in which vaccine assessment and decision-making pathways can be enhanced. This policy paper emphasises the need to improve the **timeliness**, **inclusiveness**, **consistency**, and **transparency** of assessments/decision-making by public authorities, and makes the following **recommendations for policy action** at national and European level:

***National level** – Vaccines Europe calls for/upon:*

I. Ministries of Health (MoHs) to **convene all relevant stakeholders** to examine national pathways for vaccine assessments and decision-making. Where improvement opportunities are identified, and after appropriate consultation, MoHs should **design and implement reforms**.

II. MoHs to ***'Review the composition, terms of reference and capacity of NITAGs*** (National Immunisation Technical Advisory Groups) *to develop evidence-based recommendations for immunization across the life course'* – in line with the World Health Organization's *European Immunization Agenda 2030*. Transparency can be embedded in NITAGs' terms of reference.

III. Finance ministries and MoHs – in view of the high social and economic value of vaccination – to ensure that **immunisation financing is sustainable**, flexible (in order to respond to rising demand) and supports the shift towards life course vaccination.

***European level** – Vaccines Europe calls for/upon:*

IV. The Council of the EU to develop and adopt a **Recommendation** on vaccination for resilient health systems. *Inter alia* this could provide non-binding guidance to governments on **best practices and methodologies** for vaccine assessments and decision-making.

V. The establishment of a European **vaccine clinical committee on health technology assessment** (HTA) to ensure appropriate implementation of the EU Regulation on HTA with respect to vaccines, including through the development of guidance on vaccine-specific clinical HTA methods / processes.

VI. The European Commission to encourage Member States to make sustainable **investments in life-course immunisation** programmes and monitor national immunisation spending / budgets (e.g. via the **European Semester** and/or the **State of Health in the EU** cycle).

[1] Laigle *et al.,* 'Vaccine market access pathways in the EU27 and the United Kingdom – analysis and recommendations for improvements', *Vaccine* 39 (2021).

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4 Principles for Enhancing Vaccine Assessment and Decision-Making Pathways

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INTRODUCTION

Vaccination programmes save millions of lives globally and generate significant economic and societal value through better individual and population health across the life course, cost savings for health systems, reduced use of antibiotics that would otherwise be needed to treat vaccine-preventable diseases, and a more healthy, productive and economically active population.[2]

While the COVID-19 experience may be unusual, national and European responses to the pandemic clearly illustrated the linkages between timely decision-making on vaccines, population health, and broader economic and societal outcomes (such as employment, poverty, and mental well-being).

The Value of Vaccination

- In Spain, hospitalisations due to chickenpox (varicella) decreased by 78% after routine vaccination of 15- to 18-month-old infants between 2006 and 2010.
- The implementation of a 90% universal chickenpox vaccination coverage could prompt total cost savings of 61% in Germany and 60% in France, mostly due to reduced workdays lost.
- A measles epidemic in Greece in 2017-18 resulted in an average of 21.2 days of absenteeism from work among healthcare professionals who acquired the disease. This resulted in an average estimated total direct cost of €3,379 per measles case and a total indirect cost of €1,359.
- Every euro invested in adult vaccination (starting at age 50) yields four times that amount in future economic revenue for government over the remaining lifetime of the cohort
- Yearly seasonal influenza vaccination can save between €248 and €332 million in healthcare costs in Europe by avoiding hospitalisations and visits to the General Practitioner.
- Vaccination against influenza can reduce hospitalisations and deaths by 45% and 38% respectively in older people with diabetes, and is associated with reduced risk of cardiovascular death
- Vaccination against hepatitis B and HPV could prevent 1.1 million cancer cases every year worldwide.

Source: the figures above are taken from Vaccines Europe factsheets on the Public Health Impact of Vaccines and the Economic Impact of Vaccines.[3] For full references, please refer to the factsheets.

A sustainable vaccines ecosystem[4] requires robust policies across the vaccine lifecycle in order to support:

- research and development of new vaccines
- horizon scanning and foresight
- optimal pathways for the assessment of vaccines and decisions on their inclusion in National Immunisation Programmes (NIPs)

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[2] M. Chan, 'The Contribution of Immunization: Saving Millions of Lives, and More', *Public Health Reports* 129, supplement 3 (2014); F. Andre *et al.* 'Vaccination greatly reduces disease, disability, death and inequity worldwide', *Bulletin of the World Health Organization* 86, 2 (2008); K. Jansen and A. Anderson, 'The role of vaccines in reducing anti-microbial resistance (AMR), *Human Vaccines and Immunotherapeutics*, 14, 9 (2018); P. Bonnani, J. Picazo, V. Remy, 'The intangible benefits of vaccination – what is the true economic value of vaccination?', *Journal of Market Access & Health Policy* 3, 1 (2015); N. Largeron *et al.,* 'Role of vaccination in the sustainability of healthcare systems', *Journal of Market Access & Health Policy*, 3, 1 (2015).

[3] Vaccines Europe, Factsheets on Public Health Impact of Vaccines and Economic Impact of Vaccines, available at: https://www.vaccineseurope.eu/news/articles/realising-the-full-value-of-vaccination.

[4] On the vaccines ecosystem, see (for example): 'The Vaccines Ecosystem' in *The Economist*: https://vaccineecosystem.economist.com/; and 'A 'Healthy' Vaccines Ecosystem' in EURACTIV: https://en.euractiv.eu/wp-content/uploads/sites/2/special-report/EA-EVENT-REPORT-MSD-V01.pdf.

- sustainable immunisation financing that reflects changing demographics
- more reliable demand forecasting
- optimisation of vaccine manufacturing and supply
- appropriate and sustainable procurement practices
- population-based services to ensure good implementation of vaccination programmes and improving rates of immunisation coverage
- efforts to strengthen vaccine confidence
- strong immunisation information systems (including registries) to support immunisation monitoring, reporting and surveillance across all age groups

As Europe begins to look beyond the COVID-19 pandemic, there is an opportunity to reflect on the ways in which the European vaccines ecosystem can be enhanced, and to take the necessary policy steps to achieve this.

This Vaccines Europe policy paper focuses on the pathways through which vaccines are assessed and decisions made on their inclusion in NIPs. These country-specific pathways are a key component of immunisation systems and resilient health systems. Enhancing their design and functioning can strengthen the vaccines ecosystem in a range of ways, including through more timely population access to vaccines, and support wider immunisation-related objectives and policies. For example:

- Implementing horizon scanning (to identify vaccines that may be licensed in the near future) can ensure that National Immunisation Technical Advisory Groups (NITAGs) – which are expert advisory committees on vaccination – and Health Technology Assessment (HTA) bodies are better prepared to assess new vaccines in a timely way. Horizon scanning can also help governments plan budgets for future vaccination programmes.[5]

- Policy action to strengthen vaccine assessment and decision-making pathways can support the shift towards life course immunisation – e.g. by ensuring that NITAGs have sufficient knowledge and expertise on adolescent and adult (in addition to paediatric) vaccination. Life course immunisation can in turn make an important contribution to healthy ageing policies across the European Union.[6]

- Transparent publication of the rationales underlying NITAG / HTA body recommendations and final policy decisions can reinforce efforts to strengthen vaccine confidence among EU citizens.

Vaccine assessment and decision-making pathways – an overview

The inclusion of vaccines in NIPs is the outcome of complex and heterogenous assessment and decision-making pathways. Two key steps that feature in all national pathways are:

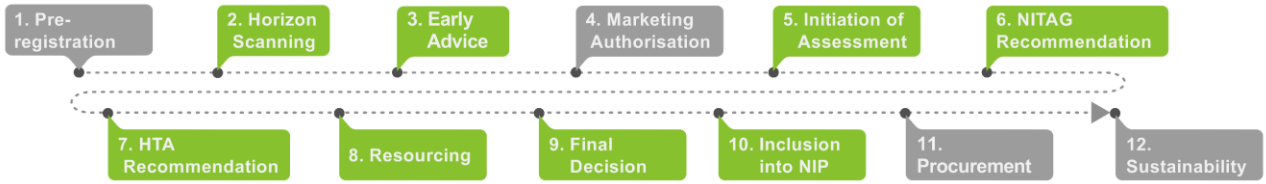
(i) **the development of evidence-based recommendations** by National Immunisation Technical Advisory Groups (NITAGs) and in some cases HTA bodies as well;

[5] R. Lawlor *et al.*, 'A review of the sustainability of vaccine funding across Europe and implications for post-COVID policymaking', *Health Policy* (2022).
[6] R.K. Philip *et al*., 'Life-course immunization as a gateway to health', *Expert Review of Vaccines* 17, 10 (2018).

(ii) **a final policy decision** on whether to include a vaccine within a NIP, followed by binding funding. The final policy decision is often (but not always) taken by the ministry of health.

Figure 1 (below) provides a generic overview of the vaccine assessment and decision-making pathway. The steps analysed and discussed in this policy paper are highlighted in green.

Figure 1: pathway for vaccine assessment and decision-making



Adapted from Laigle et al. (2021)

However, there are significant variations in country-specific processes and practices, including as regards:

- the roles performed by different national bodies
- the timeliness of assessments and decision-making (outlined in the section on Timeliness below)
- the methodologies used by NITAGs and HTA bodies to assess vaccines
- the transparency of the recommendation and decision-making process; and
- approaches to immunisation financing

Philippe Duclos of the Department of Immunization, Vaccines and Biologicals at the World Health Organization has written that: '*Key to improving routine immunization programmes and sustainably introducing new vaccines and immunization technologies is for countries to ensure that they have the necessary evidence and clear processes to enable informed decision making in the establishment of immunization programme priorities and the introduction of new programme strategies, vaccines and technologies'*.[7]

Research by Vaccines Europe, which has been published in the journal Vaccine[8], has outlined a range of opportunities to improve national pathways for vaccine assessment and decision-making, which are discussed further in this policy paper, including recommendations for policy action at national and EU level.

European policy context: EU & WHO Europe

The organisation and delivery of health services is a Member State responsibility. However, the EU treaties provide EU institutions and agencies with supporting competence in combatting serious cross-border threats to health, as well as in the 'fight against major health scourges'.[9] Even before

[7] P. Duclos, 'National Immunization Technical Advisory Groups (NITAGs): Guidance for their establishment and strengthening', *Vaccine* 28, Supplement 1 (2010).
[8] Laigle *et al.* (2021).
[9] Article 168, Treaty on the Functioning of the European Union, available at: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A12008E168.

the COVID-19 pandemic, which has catalysed EU action on health in a number of areas, the EU was engaged in a variety of activities focused specifically on vaccines. These included:

- The 2018 European Commission Communication and EU Council Recommendation on strengthened cooperation against vaccine-preventable diseases (together with Commission's implementation roadmap), which responded to concerns about declining vaccination coverage rates in the EU and subsequent outbreaks of vaccine-preventable diseases. *Inter alia* the Council Recommendation called for the EU to *'facilitate technical cooperation between public health authorities in support of the work conducted by NITAGs and affiliated bodies'*.
- The EU Joint Action on Vaccination, which aimed to strengthen cooperation between Member States in the fight against vaccine-preventable diseases, as well as the European Vaccination Information Portal – one purpose of which is to help combat the growth of vaccine hesitancy.
- A voluntary collaboration between NITAGs, initiated by the European Centre for Disease Prevention and Control (ECDC) in 2018, with the aim of developing a *'system for the exchange of existing and new scientific evidence and the joint generation of up-to-date scientific evidence'*.
- EU-funded projects such as DRIVE, IMMUNION, RESCEU and RIVER-EU:
    - DRIVE (Development of Robust and Innovative Vaccines Effectiveness) is a public private partnership that aims to advance European cooperation in influenza vaccine effectiveness studies.
    - IMMUNION aims to improve vaccine uptake by providing better vaccine education to healthcare professionals, and better information to the general public.
    - RESCEU on Human Respiratory Syncytial Virus (RSV). The project (which concluded in September 2022) aimed to integrate and exploit existing knowledge/data to provide greater insights into the impact of RSV on health systems and societies throughout Europe, and to actively engage stakeholders in order to improve strategic planning and decision-making.
    - RIVER-EU aims to reduce inequalities in vaccine uptake by improving access to vaccination services for children and adolescents in underserved communities.

Looking ahead, the EU Regulation on Health Technology Assessment (hereafter EU Regulation on HTA), which will be implemented progressively (with joint scientific consultations for all products commencing in 2025, and joint clinical assessments for vaccines beginning in 2030) will significantly alter the framework for clinical assessment of vaccines in the EU. It is therefore crucial not only that the Regulation is well implemented, taking into account the unique features of vaccines, but also that Member States begin to prepare for this change.

More broadly, it should be noted that equitable access to health care is central to the Pharmaceutical Strategy for Europe. As will be discussed further below, significant cross-country variation in the timeliness of vaccine assessment and decision-making pathways raises important equity concerns.

The World Health Organization's European Immunization Agenda 2030 (EIA 2030), released in November 2021, contains three 'Impact goals':

(i) reduce mortality and morbidity caused by diseases preventable through vaccination;
(ii) increase equitable access to new and existing vaccines for everyone regardless of age, identity and geographic location;
(iii) strengthen primary health care and thereby contribute to achieving Universal Health Coverage and sustainable development.

Strategic Priority 4 of EIA 2030 focuses on life-course immunisation and the need to *'develop or update immunization policies to strengthen life course immunization approaches'*.

PRINCIPLES TO GUIDE POLICY ACTION

The proposals in this policy paper are structured around four principles, which should guide and inform efforts to improve vaccine assessment and decision-making: ***timeliness***, ***inclusivity***, ***consistency***, and ***transparency*** in relation to the activities/decisions of public bodies. While the principles are discussed separately below, they are closely connected, and certain themes (such as sustainable immunisation financing) can be considered relevant to more than one principle.

The evidence provided by VE research (supplemented by other, closely related studies) highlights that, in many cases, the four principles are not fully reflected in the design and functioning of vaccine assessment and decision-making pathways. Furthermore, if all four principles were followed, a convergence in national practices could be expected, as well as more timely population access to new vaccines.

I. Timeliness

Timely assessments and decision-making on vaccines should be a core feature of national immunisation systems in all EU Member States. Delays in population access (defined here as the implementation of mandatory funding, either via public procurement or reimbursement, following the inclusion of a vaccine in the NIP) to new vaccines may have detrimental consequences for the health of individuals and populations more broadly.

However, an analysis conducted by Vaccines Europe confirms the findings of previous studies in highlighting significant cross-country variation in the timeliness of vaccine assessments and decision-making.[10]

Timeliness was assessed in relation to the three milestones below (with population access defined as the date on which funding was effectively implemented:

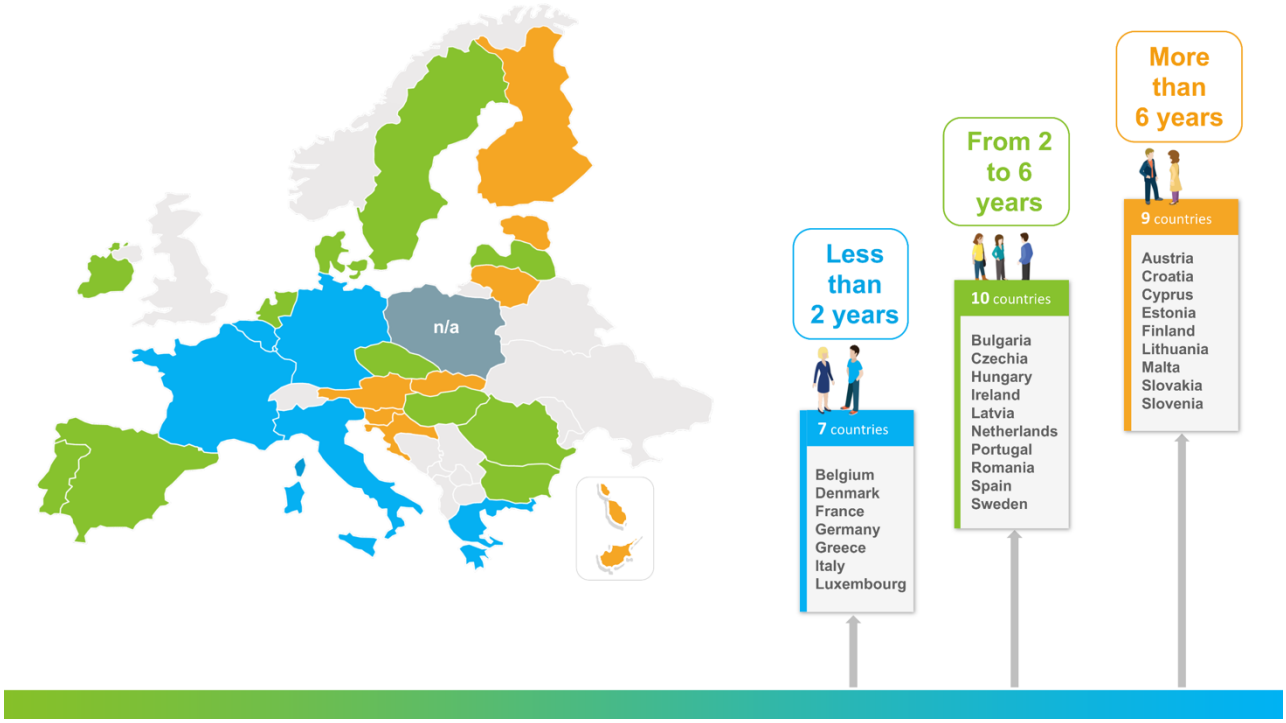
(i) marketing authorisation to NITAG recommendation
(ii) NITAG recommendation to funding
(iii) marketing authorisation to funding *(hereafter 'time to population access')*

The analysis of median time to population access (TTPA) across EU Member States (MS), illustrated in Figure 2 below, indicates that:

[10] S. Sheikh *et al.,* 'A Report on the Status of Vaccination in Europe', *Vaccine* 36, 33 (2018); P. Blank *et al.*, *Population access to new vaccines in European countries*, *Vaccine* 31, 27 (2013).

- in seven EU MS (BE, DK, FR, DE, GR, IT, LU), TTPA is less than two years.
- in the majority of EU MS TTPA exceeds two years.
- in nine EU MS (AT, HR, CY, EE, FI, LT, MT, SK, SI), TTPA is more than six years.[11]

Figure 2: Variation in time to population access for vaccines across EU Member States



Adapted from Laigle et al. (2021)

TTPA analysis methodology

Quantitative data ('vaccine range time') was obtained from vaccine industry experts for each country.

TTPA data was obtained and analysed for three vaccines in particular:

- a pneumococcal vaccine (PCV13)
- a human papilloma virus (HPV) vaccine (Gardasil 4), and
- a quadrivalent influenza vaccine (Fluarix Quadrivalent; Fluarix Tetra for France; Influsplit Tetra for Germany).

The selection rationale was to include vaccines targeting widespread and/or common diseases adopted for routine use in multiple EU Member States, across a spectrum of populations (pediatric, adolescent, and adult).

Range and 95% confidence intervals (CI) were calculated. Median TTPA for the three vaccines was compared with the range times provided by vaccine industry experts (for consistency), and with the data presented in the existing literature.

[11] Laigle *et al.* (2021).

The findings above not only point to significant and undue delay in vaccine assessments and decision-making in many countries, they also raise equity concerns – with the inclusion of vaccines in NIPs occurring much sooner in some EU Member States than others.

The timeframes in the majority of countries also significantly exceed the 180-day limit provided for by the EU Directive relating to the transparency of measures regulating the price of medicinal products.[12] It is therefore vital that countries take steps to introduce and observe clear timeframes for decision-making on the inclusion of vaccines in NIPs.

In order to improve the timeliness of vaccine assessment and decision-making pathways, Vaccines Europe proposes policy action in three main areas: i. strengthening NITAG capacities and cooperation with HTA bodies; ii. the implementation of processes for horizon scanning and early advice (where these do not currently exist); and iii. sustainable immunisation financing. Each of these points is discussed further below.

i. Strengthening NITAG capacities & cooperation with HTA bodies

The need to strengthen NITAGs is clearly highlighted in WHO's *European Immunization Agenda 2030* – specifically in order to support the development of 'evidence based policy recommendations for the introduction of vaccines across the life course'.

To ensure timeliness, NITAGs must have access to sufficient human and technical resources, as well as the capacity to undertake several assessments in parallel. Vaccine assessments require multi-disciplinary expertise, including epidemiology (incidence, prevalence, etc), clinical aspects (efficacy/effectiveness), public health aspects, value for money (cost-effectiveness), and patient/population preferences.[13] These competencies should reflect the needs of life-course immunisation, including expertise relevant to paediatric, adolescent and adult vaccination.

The respective roles of NITAGs and HTA bodies should be clearly defined. Collaboration *between* NITAGs and HTA bodies is also needed to avoid duplication and/or discrepancies, which may increase TTPA and disparities across countries. In this context (and as will be discussed further below), there should also be no informal prioritisation of vaccines for assessment based on budgetary considerations.

European-level cooperation between NITAGs offers clear potential to improve efficiency and reduce duplication, particularly with respect to evidence generation and analysis.[14] For that reason, Vaccines Europe strongly supports the continuation and enhancement of the voluntary collaboration between NITAGs initiated by ECDC in 2018, as well as revision of the ECDC mandate to strengthen information sharing and cooperation with relevant bodies at national level.

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[12] Council Directive 89/105/EEC of 21 December 1988 relating to the transparency of measures regulating the prices of medicinal products for human use and their inclusion in the scope of national health insurance systems: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A31989L0105.

[13] See G.W. Ricciardi *et al.*, 'Comparison of NITAG policies and working processes in selected developed countries', *Vaccine* 33, 1 (2015); and Privor-Drumm *et al.* 'Archetype analysis of older adult immunization decision-making and implementation in 34 countries', *Vaccine* 38, 26 (2020).

[14] ECDC, *Current practices in immunization policymaking in European countries*, 2015: https://www.ecdc.europa.eu/en/publications-data/current-practices-immunisation-policymaking-european-countries.

At the same time, there are essential elements in the assessment of vaccines which are specific to countries and cooperation between NITAGs and/or other national bodies must take account of national and sub-national specificities, as well as the decisional competence of Member States on matters related to health.

ii. Horizon scanning and early advice

Vaccines Europe's research identified differences in the extent to which national pathways include forward-looking processes, such as horizon scanning and the provision of early advice to vaccine manufacturers – both of which can improve the efficiency of assessments and decision-making.

- Horizon scanning involves the identification of vaccines that may be licensed in the near future and should ideally be conducted once or twice year.
- Early advice to vaccine manufacturers on candidate vaccines may take one of two forms:
  - *Formal early advice* – including whether a vaccine is eligible, the level of evidence required, confirmation of PICO (population, intervention, comparison, outcome) question, documentation and timelines, and industrial capacity preparedness. Within the context of the EU Regulation on HTA, this kind of advice may occur at EU level and/or at local level.
  - *Informal early advice* – usually provided verbally in face-to-face meetings (as per the country practice).

Horizon scanning and early advice can contribute to the timeliness of vaccine assessment and decision-making pathways by ensuring that the preparatory and evidence requirements (notably epidemiological, clinical, and modelling evidence) of NITAGs and HTA bodies are identified and understood at an early stage in the clinical development of new vaccines, and that appropriate additional evidence can be generated where needed.

Horizon scanning can also assist governments in planning immunisation budgets, and thereby contribute to sustainable immunisation financing.[15]

Vaccines Europe's research found that:

- Horizon scanning is conducted in only 14 of 27 EU Member States (BE, HR, CY, DK, FI, FR, DE, IE, LU, MT, NL, PT, ES, SE)*
- Formal early advice is provided in only five EU Member States (DK, FR, NL, PL, PT)
- Informal early advice is provided in a further seven Member States (AT, BE, IE, IT, SK, ES, SE)

** N.B. there are differences between countries in the way that horizon scanning is implemented, which can reflect broader differences in the organisation of health systems.*

At the time of VE's research, early advice was not provided in 15 EU Member States – with potentially negative repercussions on the timeliness and efficiency of vaccine assessments and decision-making.

[15] R. Lawlor *et al.* (2022).

iii. Sustainable immunisation financing

Immunisation financing includes both the level of funding dedicated to immunisation systems, and how the funds are used to deliver vaccination programmes. Many European countries spend less than 0.5% of GDP on prevention and (despite the significant economic, social and health benefits associated with immunisation programmes) vaccines account for a very small proportion of total health spending.[16]

An analysis of 25 EU Member States (excluding Belgium and Greece, for which data was not available) plus the UK found that more than three quarters of countries spend less than 0.5% of their healthcare budget on immunisation.[17]

Sustainable immunisation financing is essential to ensure high performing immunisation systems, including timely decisions on the inclusion of vaccines in NIPs. Governments should ensure sufficient resources are in place to include all recommended vaccines in NIPs.

Immunisation/prevention budgets should also be protected from fiscal consolidation measures, such as occurred following the 2007/08 financial crisis. Then, per capita public health spending fell in numerous EU countries,[18] with even more marked reductions in per capita vaccination expenditure in some cases.[19]

Sustainable immunisation financing should reflect the shift towards life course immunisation, and ensure budget flexibility, so that spending can be increased at times of increased demand for immunisation – as will likely be the case with COVID-19 vaccines in an endemic phase and an increasing number of available vaccines to prevent adults suffering from communicable diseases.

It follows that robust forecasting regarding the evolution of immunisation programmes and, thereby, of demand is an essential component of sustainable immunisation financing.[20] Demand forecasting can in turn be enabled by the implementation of horizon scanning.

In order to ensure the optimal performance of immunisation systems, countries should invest in monitoring and reporting, as well as regular performance assessment of immunisation programmes. EU guidance on options for appropriate methodologies and indicators would be beneficial – building on previous exchanges of best practice on health systems performance assessment.[21]

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[16] O. Ethgen *et al.*, Vaccination budget in Europe: an update, *Human Vaccines and Immunotherapies* 14, 12 (2018); P. Faivre *et al.*, 'Immunisation funding across 28 European countries', *Expert Review of Vaccines* 20, 6 (2021).
[17] Faivre *et al.* (2021). This finding was consistent with O. Ethgen, F. Baron-Papillon, and M. Cornier, 'How much money is spent on vaccines across Western European countries?' *Human Vaccines and Immunotherapeutics*, 12, 8 (2016); and Ethgen *et al.* (2018).
[18] S. Thompson *et al.*, 'Economic crisis, health systems and health in Europe: impact and implications for policy', Policy Summary, WHO Europe and European Observatory on Health Systems (2014).
[19] Ethgen *et al.* (2018).
[20] Lawlor *et al.* (2022).
[21] See European Commission, 'Health Systems Performance Assessment': https://ec.europa.eu/health/health-systems-performance-assessment_en.

II. Inclusiveness

NITAGs and HTA bodies should ensure there are mechanisms for engagement and consultation with all relevant vaccines stakeholders. That includes: scientific and medical experts; wider health care professionals (doctors, nurses and pharmacists); civil society organisations (CSOs – such as public health advocates and organisations representing patients, carers, parents and consumers); and vaccine manufacturers.

Consultation with stakeholder categories not formally included in the work of NITAGs and HTA bodies is particularly important. For vaccine manufacturers, important areas for consultation include: the possibility to submit an application for vaccine assessment, recommendation and funding; the ability to submit data; the possibility to attend pre-scoping meetings (PICO alignment) and formal hearing/discussion platforms during the decision process.

Alongside mechanisms for stakeholder consultation, formal civil society *participation* in NITAGs should be positively pursued. While VE research did not specifically investigate the composition of NITAGs, a previous comparison of NITAG policies and working practices in 13 developed countries (including 8 EU Member States), indicated that formal civil society participation in NITAGs is relatively uncommon.

There are positive examples, however: in France patient representatives are involved in the NITAG as well as HTA commissions;[22] in Australia and the United States, a consumer representative is included as a member of the NITAG.[23] In the US also, the Advisory Committee on Immunization Practices provides opportunity for written and oral public comment before making vaccine recommendations.[24]

Involvement of CSOs in the work of NITAGs would broaden the range of knowledge and expertise available to NITAGs without altering the scientific character of their assessments/recommendations. For example: expertise in relation to the causes of (and potential responses to) vaccine hesitancy, as well as how to improve vaccine uptake among vulnerable groups.

Civil society participation in NITAGs can also empower CSOs by bringing them closer to vaccine assessment and decision-making methods and processes – thus enabling them to contribute to knowledge and information sharing across the vaccines ecosystem, including the general public. That can be particularly beneficial in view of efforts to strengthen vaccine confidence and improve awareness on the benefits of life course immunisation.

[22] For the composition of the French NITAG, see HAS website: https://www.has-sante.fr/jcms/c_2755844/en/commission-technique-des-vaccinations#toc_1_2.
[23] Ricciardi *et al.* (2015).
[24] See 'Role of the Advisory Committee on Immunization Practices in CDC's Vaccine Recommendations': https://www.cdc.gov/vaccines/acip/committee/role-vaccine-recommendations.html.

III. Consistency

In its 2018 Communication on vaccine-preventable diseases, the European Commission called for action to: 'Strengthen the efficiency *and consistency* of decision making on vaccines [and] vaccination policies'.

While recognising that the organisation of health systems (including immunisation systems) is a national competence, this paper highlights the need for consistency in two main areas:

i. ***core procedures*** that should form part of vaccine assessment & decision-making pathways in all countries
ii. ***the methods and approaches*** used for vaccine assessments

In relation to the second area, the EU HTA Regulation is particularly relevant as it will alter the framework for the clinical assessment of vaccines and, provided the regulation is well implemented, has the potential to contribute to greater consistency in the way vaccines are assessed across the European Union.

i. Core procedures

Consistency of national pathways does not imply harmonisation. There will remain differences between Member States that result from differences in health systems and settings. However, as discussed in other sections of this paper, there are a number of procedures and practices that should feature in all national pathways.

In addition to evidence-based recommendations and final policy decisions, core procedures should include: horizon scanning and mechanisms for early advice on candidate vaccines; procedures for stakeholder engagement; consultation and participation; and transparency (discussed in section IV below).

ii. Methods and approaches to vaccine assessment

Within regard to the methods and approaches used for the assessment of vaccines, there is a need for greater consistency both within countries and between them.

A key finding of VE's research was that, in addition to public health and clinical factors[25], budget impact was a key recommendation driver for NITAGs in nine EU Member States (AT, BG, CY, CZ, HU, LT, MT, NL, ES).[26] However, given that judgements related to vaccination budgets are inherently political – involving questions about the appropriate use of public finances – it is important to consider whether budgetary considerations should fall within the remit of NITAGs or rather be left for the final policy decision.

Vaccines Europe's position is that NITAG recommendations should be driven fundamentally by the clinical aspects of new vaccines and public health considerations. To ensure appropriate lines of political accountability, budgetary impact should become relevant only in the final decision stage.

[25] More specifically: disease burden and disease severity; vaccine efficacy, effectiveness and safety; and cost-effectiveness. See for example: Duclos (2010); and Ricciardi *et al.* (2015).
[26] Laigle *et al*. (2021).

It follows that there should be no *de facto* prioritisation of vaccines for assessment by NITAGs / HTA bodies. Similarly, and in line with the emphasis on life course immunisation in the WHO *European Immunisation Agenda 2030*, there should also be no restriction on the assessment of vaccines based upon the demographic target group.

Finally, it should be noted that traditional cost-effectiveness analyses, which are used to assess value for money, have limitations in relation to the assessment of vaccines. For example, in many EU countries, cost-effectiveness analyses do not accurately capture the broad socio-economic benefits of vaccination programmes – such as benefits associated with employment, productivity and equity.[27] Furthermore, current cost-effectiveness analyses may not capture longer-term critical benefits provided by vaccines, such as reduction of antimicrobial resistance and antibiotic consumption.

iii. EU joint clinical HTA for vaccines

In addition to reducing the analytical workload confronting NITAGs and HTA bodies, the EU Regulation on HTA can make a significant contribution to greater consistency in the clinical assessment of vaccines. However, there are two pre-requisites: first, that the unique features of vaccines are taken into account in the implementation of the Regulation; and second, that national authorities then use the joint clinical assessments as the core of their own clinical assessments.

To help ensure that the Regulation is well implemented in the case of vaccines, Vaccines Europe has proposed, in a dedicated position paper on Joint Clinical HTA for vaccines, that:

1. *The establishment of European vaccine clinical HTA committee* – reflecting vaccine specific expertise and including all relevant stakeholders: academics, NITAGs, HTABs, ECDC, civil society.
2. *Development of guidance on vaccine specific clinical HTA methodologies and processes* – with the goal of supporting rapid implementation of effective immunisation programmes.
3. *Continuous vaccines industry engagement* – the Vaccines Industry should be closely associated with the development of a vaccine-specific clinical assessment methodology and processes. This should be based on transparent and official procedures for dialogue, consultation and exchange within appropriate and transparent venues.

[27] See for example M. Postma *et al.* 'Capturing the value of vaccination within health technology assessment and health economics: Country analysis and priority value concepts', *Vaccine* 40, 30 (2022)

IV. Transparency

Transparency is a fundamental principle for the governance of health systems and is especially relevant for the vaccines ecosystem where vaccine hesitancy is a growing challenge. For example, in the context of a research project on NITAG practices led by Professor Walter Ricciardi, an expert panel expressed the opinion that:

'NITAG appraisals should be better reported to the general public and the overall information about vaccines should be enhanced. There is a need to provide more information to the public and health councils on reasons for no recommendation (e.g., lack of data, lack of budget, etc.) in order not to jeopardize trust in vaccines.'[28]

Transparency of assessments and decision-making can also support greater accountability in vaccine decision-making, including by contributing to a better understanding of the reasons for cross-country variation in the content of NIPs and TTPA.

Transparency should encompass:

- clear definition of the roles played by different actors and bodies (e.g., NITAGs, HTA bodies, Ministries of Health, etc);
- publication of a formal decision-analysis framework so that all stakeholders can understand the process and methodology being applied;
- publication of recommendations and final decisions, including the underlying rationale;[29]
- publication of NITAG/HTA body work programmes, meeting agendas and minutes.

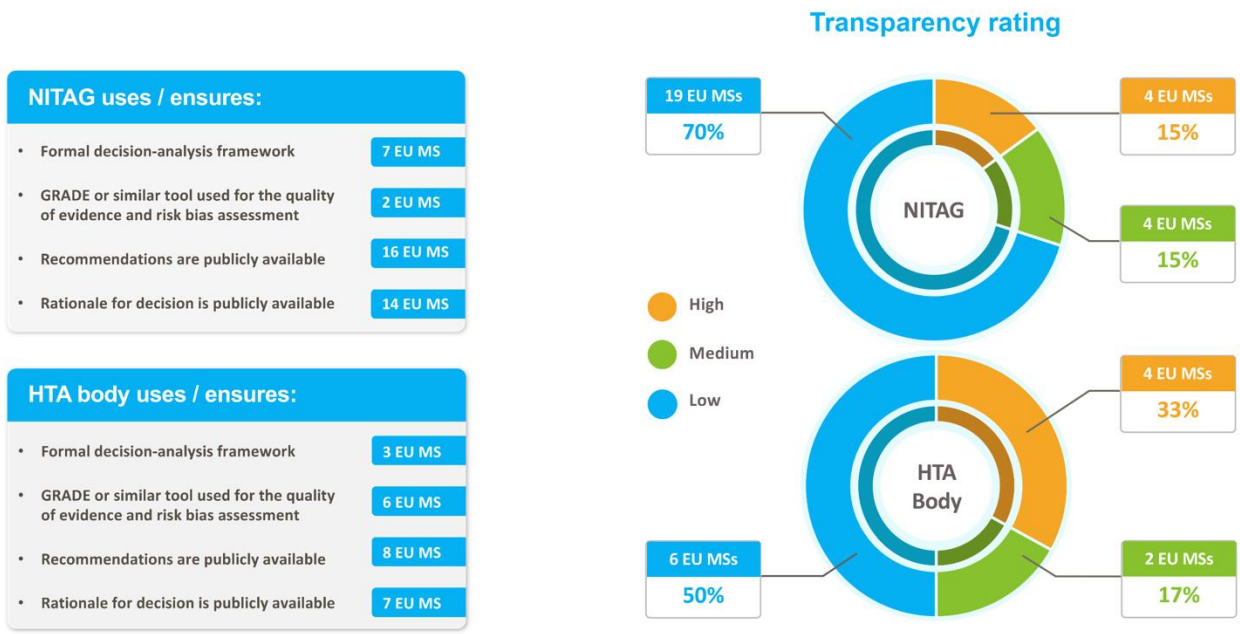
As part of its evaluation of national vaccines pathways, Vaccines Europe rated the transparency of NITAG and HTA body (HTAB) assessment and decision-making processes based on three criteria:

1) a formal decision-analysis framework is in place;
2) presence of a systematic approach for evidence appraisal; and
3) publication of the decision with rationale.

The level of transparency was considered low if 0 or 1 criterion was met; medium if 2 criteria were met; and high if all 3 criteria were met. Using this rating methodology, it was found that: 70% of NITAGs and 50% of HTABs have a low level of transparency; just 15% of NITAGs and a third of HTABs were found to have a high level of transparency – that is to say, they fulfilled all three of the criteria outlined above (see Figure 3 below).

[28] Ricciardi *et al.* (2015).
[29] See G. Bencina *et al.*, 'Recommendations and Health Technology Assessment (HTA) landscape evaluation for pediatric pneumococcal conjugate vaccines (PCV) in Europe: A systematic literature review', *Human Vaccines and Immunotherapies* 18, 5 (2022); Duclos (2010).

Figure 3: Transparency ratings for NITAGs & HTA bodies



Analysis based on 27 NITAGs (incl. UK, which was an EU MS at the time of the research, but not Romania where a NITAG had not yet been established), and 12 countries where HTA body also conducts an assessment.

Adapted from Laigle et al. (2021)

VACCINES EUROPE RECOMMENDATIONS

National level – VE calls for/upon:

I. **Ministries of Health** (MoHs) to convene all relevant stakeholders (NITAGs, HTABs, scientific experts, medical societies, civil society organisations, and vaccine manufacturers) to examine the functioning of national pathways for vaccine assessment and decision-making. Particular attention should be paid to the timeliness, transparency, consistency, and inclusiveness of these pathways, including by ensuring that the roles and mandates of different bodies are clear, and that the methods used for the assessment of vaccines are appropriate based on current scientific knowledge. Where areas for improvement are identified, further stakeholder consultation is requested as a precursor to MoHs designing and implementing appropriate reforms.

II. MoHs to *'**Review the composition, terms of reference and capacity of NITAGs** to develop evidence-based recommendations for immunization across the life course"* (in line with WHO Europe's *Immunization Agenda 2030*). Particular attention should be paid to the human and technical resources available to NITAGs with a view to ensuring timely and robust assessments/recommendations. A requirement to publish recommendation rationales could be embedded in NITAG terms of reference.

III. Finance ministries and MoHs – in view of the broad public health, economic and social value of vaccination, the relatively small share of total health spending accounted for by immunisation programmes, and the negative impact that fiscal consolidation measures can have on population access to vaccines – to ensure that **immunisation financing is sustainable, flexible** (in order to respond to increased demand for vaccines) and **supports the shift towards life course vaccination**, ensuring equitable access to vaccines across demographic groups.

European level – VE calls for/upon:

IV. The Council of the EU to develop and adopt a Recommendation on vaccination for resilient health systems that builds upon European Commission's 2018 Communication on strengthened cooperation against vaccine preventable diseases, which highlighted the need to *'Strengthen the efficiency and consistency of decision making on vaccines'*, as well as the Council Recommendation of the same year. *Inter alia* the Recommendation could provide non-binding guidance to national governments on **best practices and methodologies** for vaccine assessments and decision-making, with the aim of ensuring more equitable and timely access to vaccines across Member States.

In line with the intention of the EU4Health programme to *'support Member States in monitoring the performance of national vaccination programmes and services'*,[30] the Recommendation could also propose indicators to monitor and assess the performance of

[30] European Health and Digital Executive Agency, EU4Health Prior Information Notices, available at: https://hadea.ec.europa.eu/news/four-eu4health-new-prior-information-notices-published-2022-02-03_en

NIPs. Alongside the number of vaccines included in an NIP, vaccination coverage rates, and progress towards life-course vaccination (through inclusion of adult vaccines in NIPs), performance indicators could cover the timeliness, inclusiveness, consistency, and transparency of vaccine pathways. For example, they could focus on:

- the time between marketing authorisation and:
  - (i) NITAG/HTA body recommendations
  - (ii) inclusion in the NIP / funding;
- key aspects of immunisation financing – e.g. whether there is a specific budget for vaccines, the percentage of the healthcare budget dedicated to vaccines, and vaccines spending *per capita*;
- whether there are mechanisms for stakeholder consultation, horizon scanning and early advice;
- whether recommendations and final decisions, including rationales, are published in an accessible way.

V. The establishment of a **European vaccine clinical HTA committee** to ensure appropriate implementation of the EU Regulation on Health Technology Assessment with respect to vaccines, including through the development of guidance on vaccine-specific clinical HTA methods and processes. The composition of the committee should reflect vaccine-specific expertise and include all relevant stakeholders: academics, NITAGs, HTA bodies, ECDC, and civil society representatives. In parallel, the **voluntary collaboration between NITAGs**, initiated by ECDC in 2018 should be continued and enhanced.

VI. The European Commission and Council of the EU to encourage Member States to make sustainable investments in life-course immunisation programmes that ensure vaccine equity within and between countries. For example, the European Commission (supported by Eurostat) could collect data on and **monitor national immunisation budgets/expenditure** – e.g. via the **European Semester** process for economic and social policy coordination and/or the **State of Health in the EU cycle** – as there is currently no standardised reporting on immunisation funding either at national or European level. Where countries have reduced (or intend to reduce) immunisation spending, action could be considered, by way of country-specific recommendations, to promote sustainable immunisation financing.

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