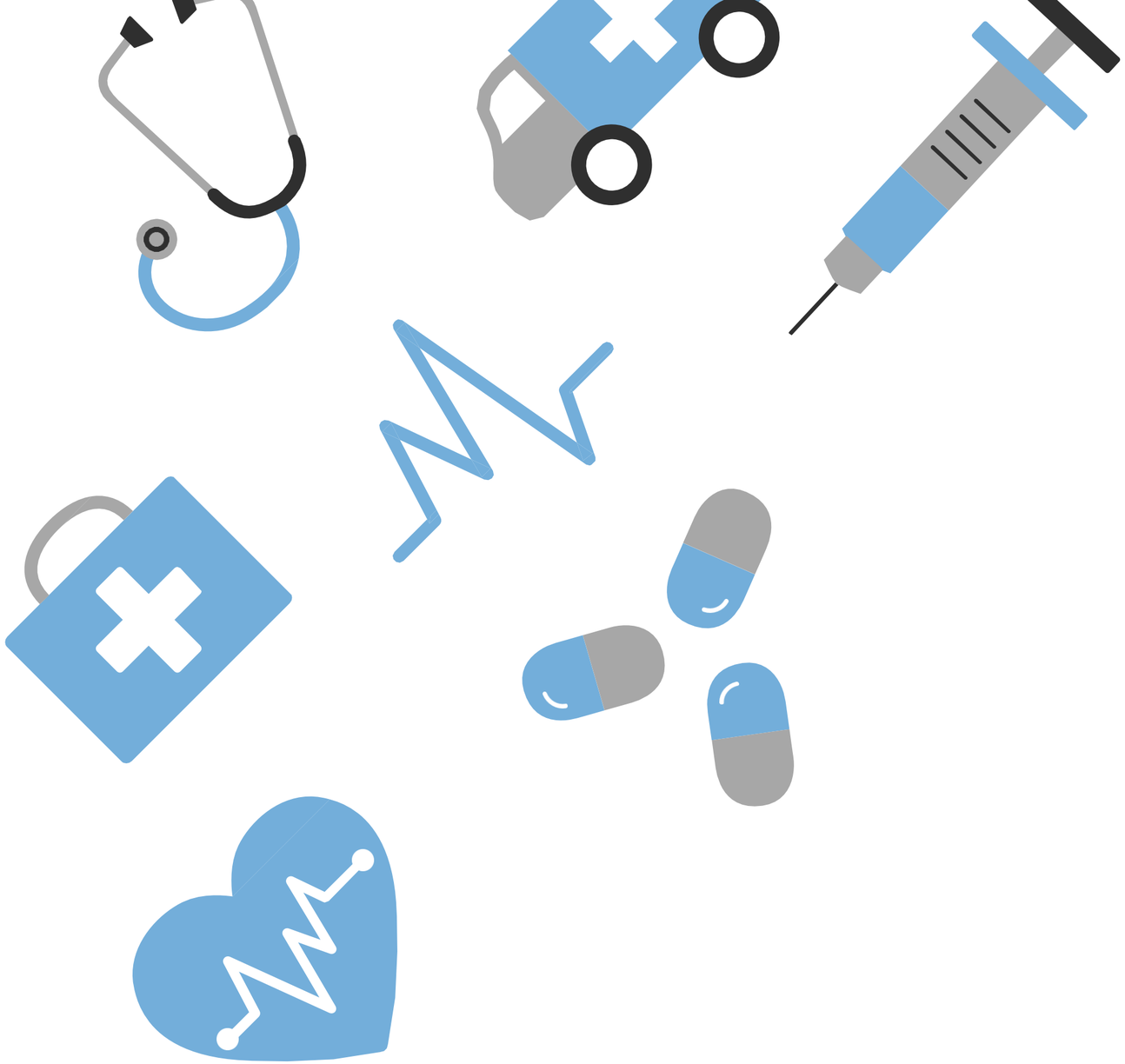

ADULT IMMUNIZATION BOARD
TECHNICAL MEETING
20-21 APRIL

IMPACT OF THE HEALTH BURDEN ON VACCINE MARKET ACCESS PATHWAYS IN THE EU27 AND THE UNITED KINGDOM

ANALYSIS AND RECOMMENDATIONS FOR IMPROVEMENTS

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Agenda

Key points for discussion

Introduction - *VMA in Europe*
Aims and scope - *Optimization of VMA across Europe*

Methodology - *2 phases*
Main results - *country cards and pathways*
Our way forward - *enhancing the Value of vaccination in 4 main pillars*

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Vaccine market access pathways in the EU27 and the United Kingdom – analysis and recommendations for improvements

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ABSTRACT

Background: Vaccine market access (VMA) pathways across the European Union (EU) and the United Kingdom (UK) are complex, lengthy, and heterogeneous, particularly when compared with pharmaceuticals. The knowledge base to inform recommendations for optimization of VMA is lacking. We therefore conducted a comprehensive evaluation of EU VMA pathways.
Methods: Research in two phases included: (1) mapping VMA pathways in each EU member state (including the UK) based on a literature review, expert interviews, and mathematical archetyping; and (2) interviews with vaccine experts to identify barriers, drivers, and recommendations for regional VMA alignments.
Results: Key steps in VMA across the EU include horizon scanning, early advice, National Immunization Technical Advisory Group (NITAG) recommendation for inclusion in national immunization programs, health technology assessment (HTA), final decision and procurement. We found significant complexity and heterogeneity, particularly for early advice, and in the roles, decision-making criteria, and transparency of NITAGs and HTA bodies. The most important drivers for rapid VMA included demonstration of disease burden and vaccine benefit (e.g., efficacy, safety, economic). Key barriers were budget limitations and complexity/clarity of VMA processes (e.g., need for national-regional consensus, clarity on process initiation, and clarity on the role of HTA). Recommendations for alignment at EU and member-state levels include information sharing, joint clinical assessment, initiatives to address funding and political barriers, and improved transparency by decision-making bodies. Early engagement with vaccine stakeholders was a key recommendation for manufacturers.
Conclusions: There is significant potential for alignment, collaboration, and improvement of VMA across the EU. Roles, responsibilities, and transparency of key bodies can be clarified. The COVID-19 pandemic response should stimulate policies to improve access to all vaccines, including routine ones, and form the foundation upon which a consistent vaccine ecosystem can be created for the EU, one that is resilient, consistent between member states, and fit for purpose.

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ADULT IMMUNIZATION BOARD TECHNICAL MEETING 20-21 APRIL

Introduction

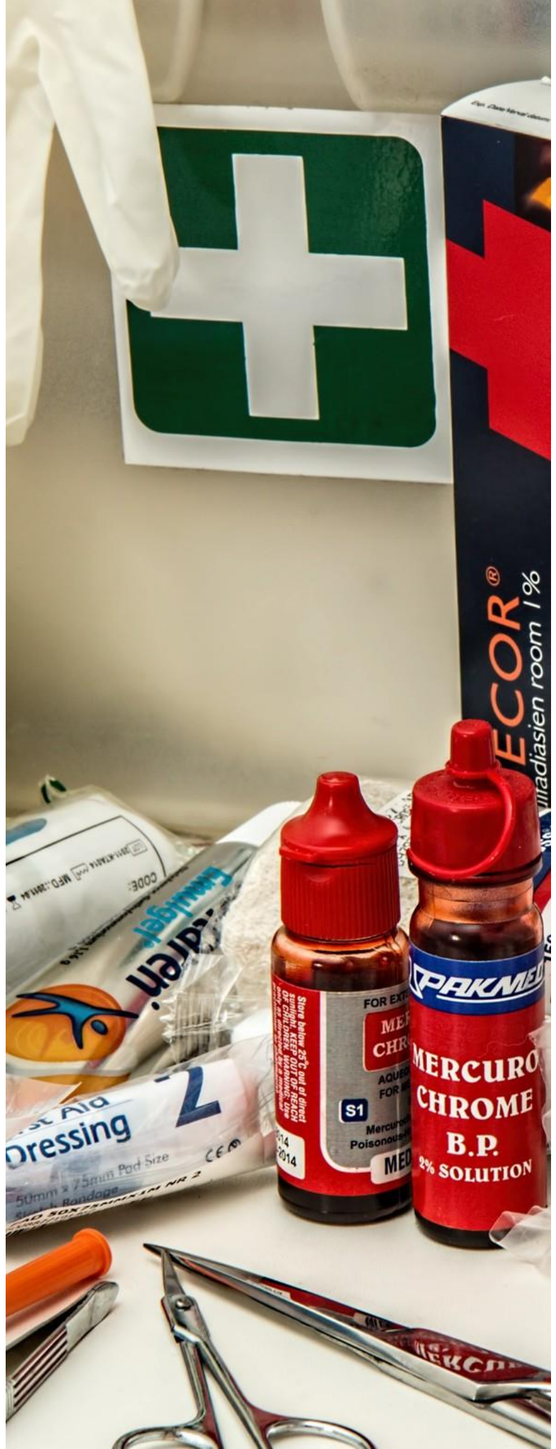
Vaccine Market Access in Europe

VMA nationally led –> NITAG –> inclusion in NIP

Significant differences in these steps –> Need for harmonization!

Fig. 3. Key features of VMA pathways in the EU28 member states. *HTA may be conducted before or in parallel with the assessment by NITAG. HTA, Health Technology Assessment; HTAB, Health Technology Assessment Body; NIP, National Immunization Program; NITAG, National Immunization Technical Advisory Group.

COVID-19 pandemic has underscored both the need and possibility for agile vaccine mobilization, even within existing VMA frameworks



Aims and scope

Optimization of VMA across Europe

Comprehensive evaluation of VMA pathways across the EU region, from marketing authorization to population access –> to provide an evidence base on which to inform policy recommendations at national and EU levels, with the goal of optimizing VMA across the region.

Phase 1

Mapping VMA pathways in each EU28 member state based on a literature review and local data collection by industry vaccine experts, culminating in mathematical archetyping and defining exemplar countries

Phase 2

Primary research with non-industry vaccine experts in exemplar countries to validate phase 1 findings --> Identification and analyses of barriers and drivers of VMA across the EU28, and recommendations for alignment

Phase 1

- Literature search
- Country card completion
- Archetype and exemplar development

Phase 2

Expert stakeholder interviews

PHASE 1

Literature review

Establish an understanding of VMA pathways and develop data collection instruments (country cards)

Selection of publications covering the key aspects of the VMA pathways in the EU28, including relevant stakeholders, processes, and time to population access (TTPA)

Embase, Medline and other relevant db

Table 1
Attributes used for preliminary mathematical clustering of EU28 VMA pathways.

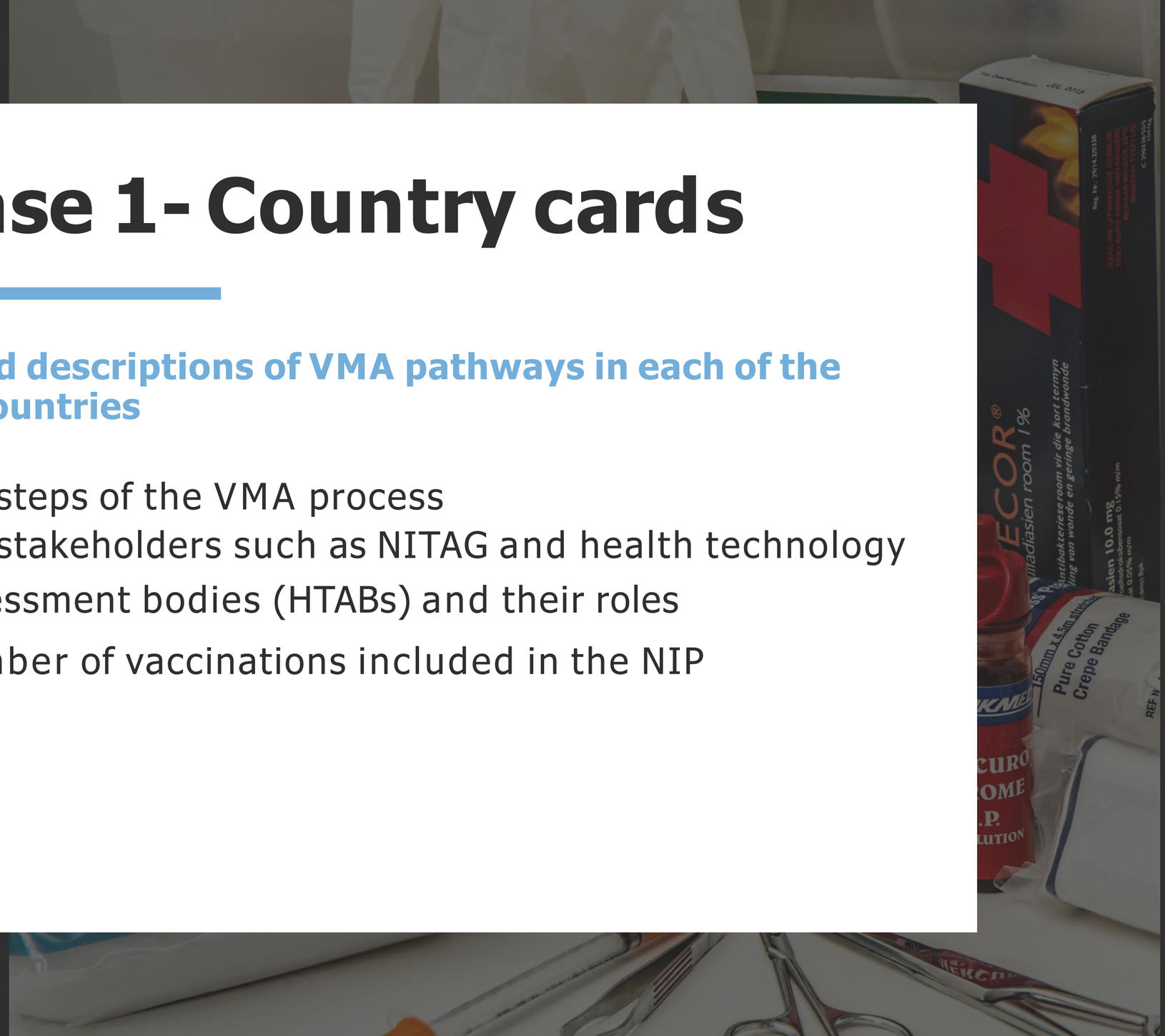
Clustering attribute
1. Applicability of horizon scanning (yes/no)
2. Availability of formal early advice (yes/no)
3. NITAG formal terms of reference (yes/no)
4. NITAG formal decision-analysis framework (yes/no)
5. Level of decision making* (national/regional/both)
6. Mandatory (binding) funding of at least one vaccine following inclusion of vaccination in immunization program (yes/no)
7. Procurement type (tender-driven/individually-driven+/both)
8. Level of tenders (national/regional/both)
9. Published award criteria and clear selection process for tenders (yes/no)
10. Number of vaccinations in immunization program (<10/10–15/>15)
11. Involvement of HTAB (yes/no)
12. NITAG preferential recommendation towards vaccine type (yes-always or usually/yes-sometimes/no)
13. NITAG main decision drivers (clinical/economic/population-based/clinical and economic/clinical and population-based/clinical and economic and population-based/other)
14. HTA main decision drivers (clinical/economic/population-based/clinical and economic/clinical and population-based/clinical and economic and population-based/other)
15. Transparency of NITAG/HTAB (low/medium/high)
16. HTA binding for the respective authority (low/medium/high)
17. Can marketing authorization holder initiate the assessment (yes/no)
18. Time to population access (<2 years/2–6 years/>6 years)

HTA, health technology assessment; HTAB, health technology assessment body; NITAG, National Immunization Technical Advisory Group.
* Issuing recommendation for inclusion into vaccination program and funding.
+ Reimbursement list for vaccines.

Phase 1- Country cards

Detailed descriptions of VMA pathways in each of the EU28 countries

- key steps of the VMA process
- key stakeholders such as NITAG and health technology assessment bodies (HTABs) and their roles
- number of vaccinations included in the NIP



Phase 1- Archetype and exemplar development

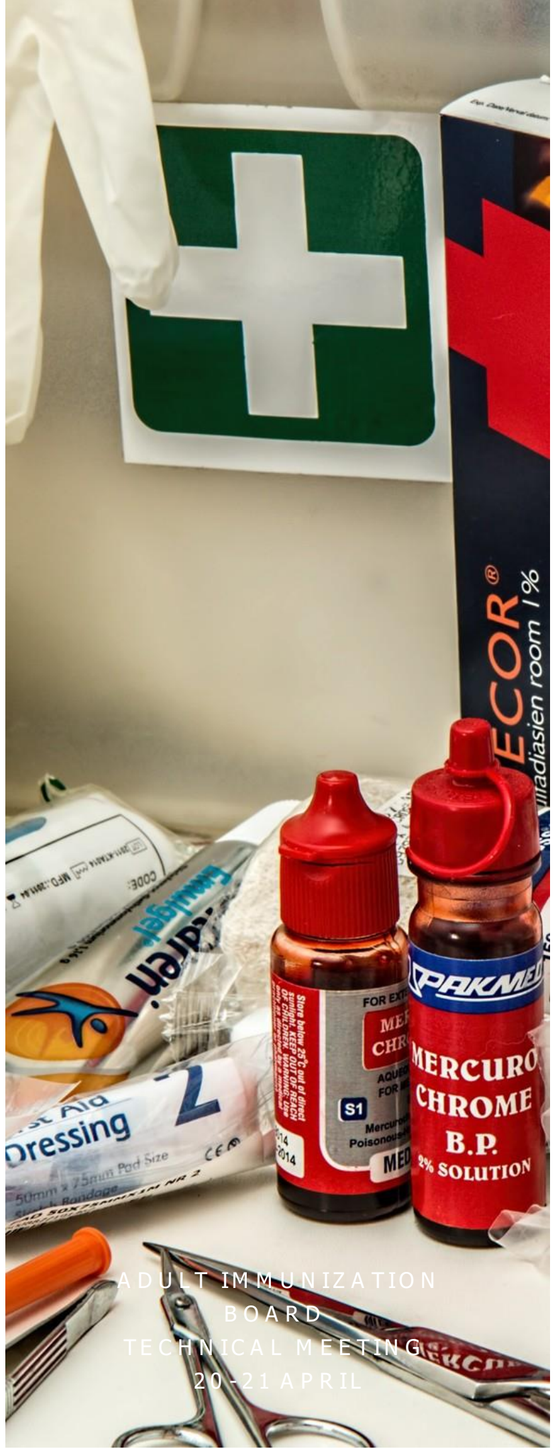
Hierarchical clustering exercise to classify the member states according to selected VMA attributes

Three attributes were selected, informed by industry vaccine experts, to perform the manual clustering:

(1)involvement of HTAB (yes/no)
(2)procurement type (formal tender-driven process and/or non-tender/individual product-driven process)
(3) level of decision-making (national and/or regional)

Exemplar countries were then selected (and cross-validated by the vaccine industry experts) for each cluster → main European (EU5) markets (France, Germany, Italy, Spain and the UK)

Created clusters were further validated by the industry experts, with final validation by non- industry experts from exemplar countries



PHASE 2

Expert stakeholder interviews

Up to two non-industry experts were recruited from each exemplar country to validate the pathway descriptions and VMA archetypes

One hour phone interview, with pre-reading material and a semi-structured questionnaire -->barriers, drivers and recommendations to improve VMA at national and EU level

Results

Literature review

17 references representing 16 original studies

Confirmation of the varying timeframes, complexity, and heterogeneity of VMA across the EU28, with numerous stakeholders involved

Some countries evaluated vaccination programs at the **population or societal levels**, rather than on individual or healthcare levels

Broader measures of vaccination value were also identified e.g., community externalities such as disease control, herd immunity, elimination, or eradication

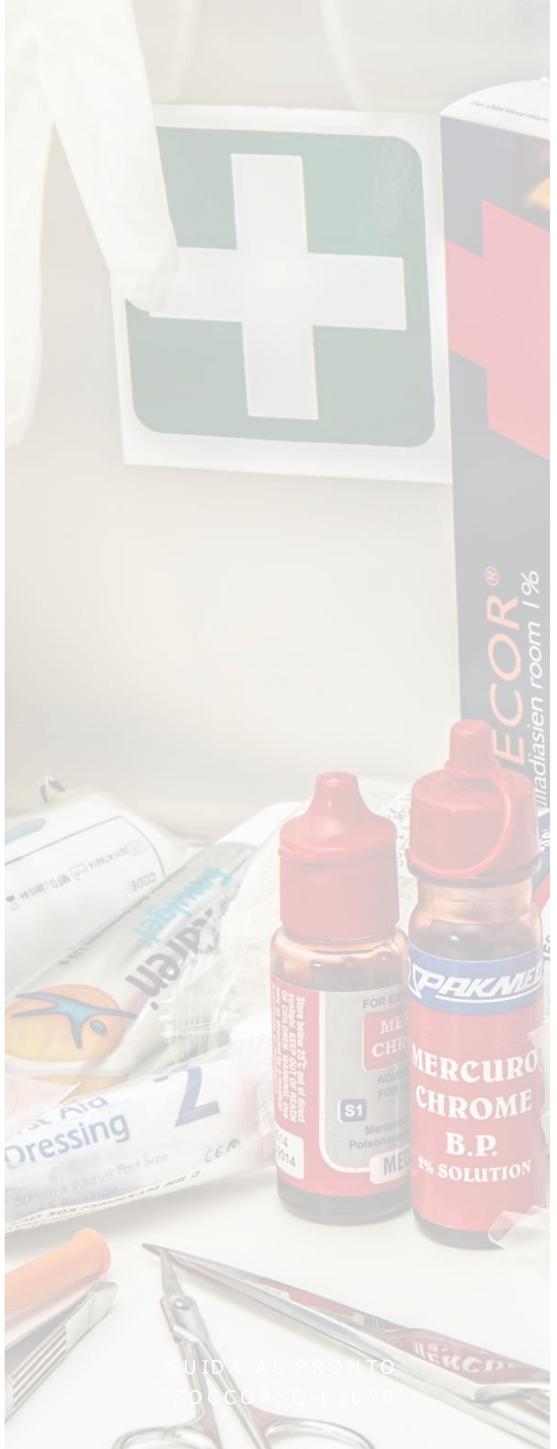
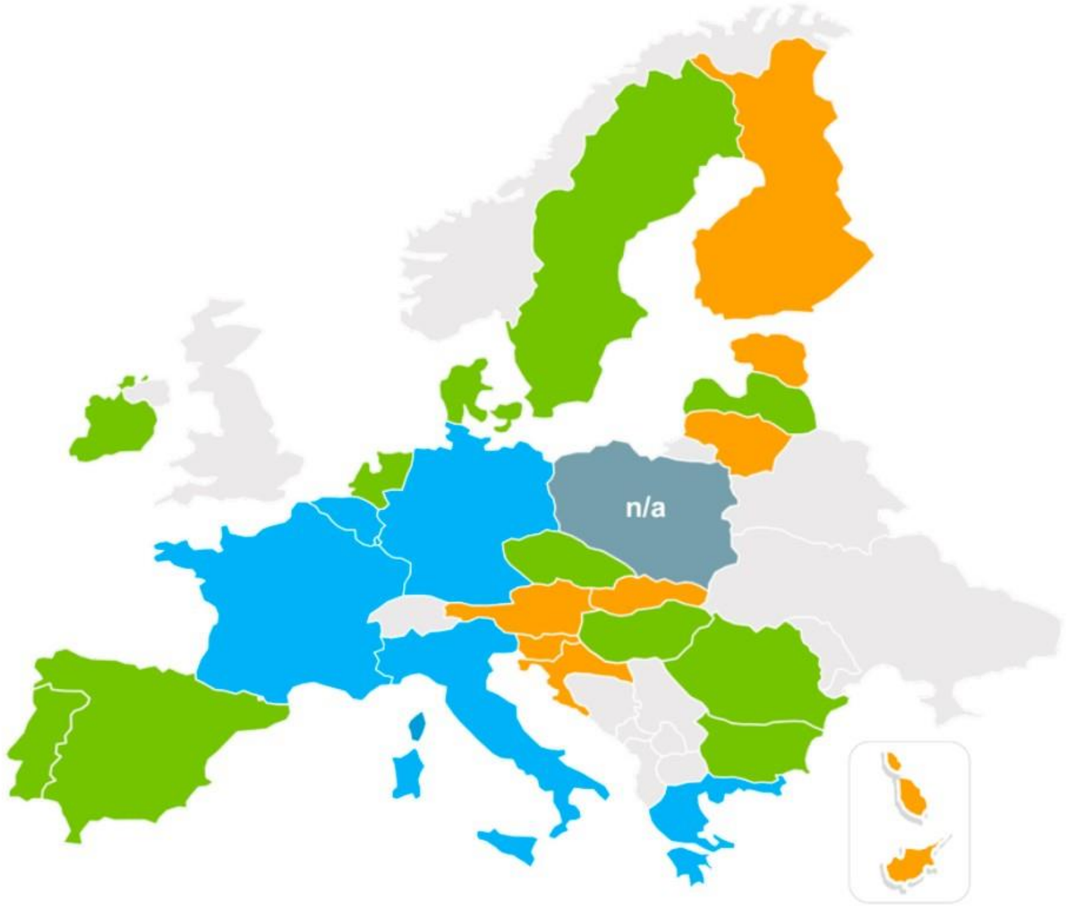


Figure 2: Variation in time to population access for vaccines across EU Member States



Less than 2 years

7 countries

Belgium
Denmark
France
Germany
Greece
Italy
Luxembourg

From 2 to 6 years

10 countries

Bulgaria
Czechia
Hungary
Ireland
Latvia
Netherlands
Portugal
Romania
Spain
Sweden

More than 6 years

9 countries

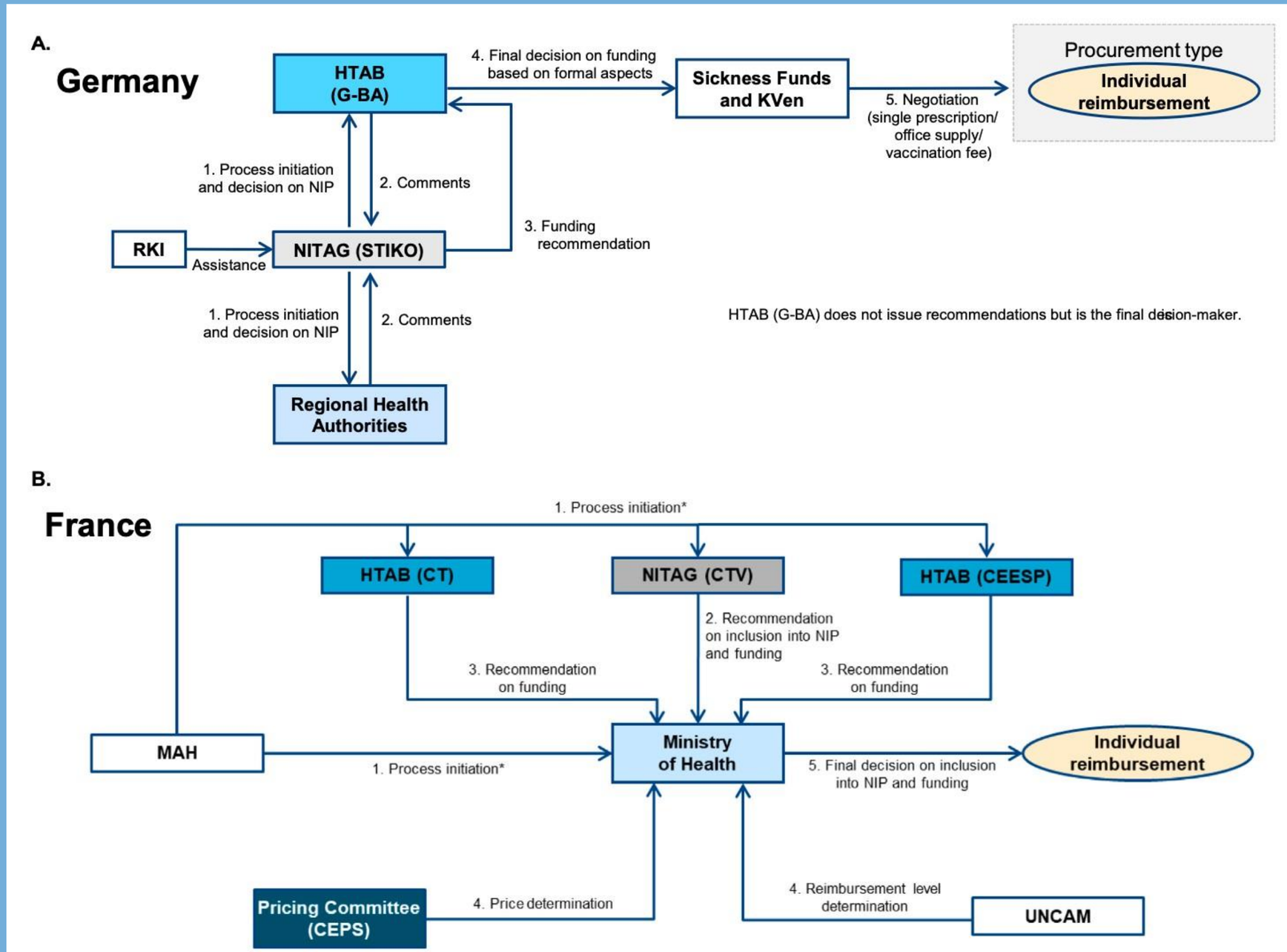
Austria
Croatia
Cyprus
Estonia
Finland
Lithuania
Malta
Slovakia
Slovenia

Adapted from Laigle et al. (2021)

Country card: Germany

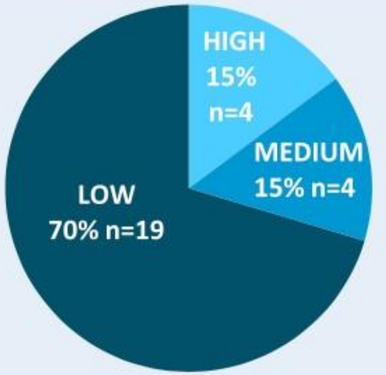
National Immunization Technical Advisory Group (NITAG)	
Name of the relevant body	NITAG: STIKO
Are there any specific eligibility criteria for vaccination programs to be assessed by NITAG?	Yes (burden of disease, medical need, availability of a licensed vaccine, vaccine profile)*
Who initiates the process?	NITAG
Does NITAG have formal terms of reference (i.e., defined purpose and structures of the organization)?	Yes
Does NITAG have a formal decision analysis framework (i.e., structured approach for decision making)?	Yes
Main decision drivers: 1 – highest relative importance 3 – lowest relative importance.	1. Burden of disease 2. Safety and tolerability 3. Public health impact
Other attributes considered by NITAG in their decision-making process	• Unmet needs • Efficacy • Effectiveness • Cost-effectiveness • Societal impact (friction cost approach for base case and human capital approach for sensitivity analysis) • Public perception of disease and/or vaccine • Transmission models • Ethical issues • Public acceptance • Organizational/implementational and equity attributes
Does NITAG make any preferential recommendations towards the vaccine type?**	Yes – sometimes
Is GRADE or any similar tool used for grading the quality of evidence and risk of bias assessment?	Yes
Are there specific timelines in place for the assessment?	No
Are NITAG recommendations and rationale publicly available?	Yes
Level of transparency†	High
WHO criteria of functionality‡	All six criteria met: • Legislative/administrative basis • Formal terms of reference • Conflict of interest policy implemented • At least five expertise areas • Meets at least once a year • Circulation of the agenda and background paper a week before meeting
Health Technology Assessment Body (HTAB)	
Name of the relevant body	G-BA (however, no HTA assessment conducted by G-BA)
Are there any specific eligibility criteria for vaccines to be assessed by the HTAB?	NA
Who initiates the process?	NA
Is the process conducted before/after/at the same time as the process conducted by NITAG?	NA
Does the HTAB have a vaccine-specific decision analysis framework in place?	NA
Main decision drivers: 1 – highest relative importance 3 – lowest relative importance	NA
Other attributes considered by the HTAB in their decision-making process	NA
Is GRADE or any similar tool used for grading the quality of evidence and risk of bias assessment?	NA
Are there specific timelines in place for the assessment?	NA
Are HTAB recommendations and rationale publicly available?	NA
Level of transparency†	NA
Is HTAB recommendation binding for respective health authorities?	NA

Key steps and stakeholders in the VMA decision-making and procurement process for Germany and France



	Horizon scanning	Early advice	Initiation of assessment	NITAG Recommendation	HTAB Recommendation	Binding funding following final decision	Final decision/ NIP inclusion	Procurement
Austria		Informal	MoH*	E(BI), Clin			N Lev	N Lev, R Lev
Belgium	1 or 2/yr	Informal	MoH*	Clin, PH	E(BI), E(CE)		N Lev	R Lev
Bulgaria				E(BI), Clin	E(BI)		N Lev	N Lev
Croatia	1 or 2/yr		PH Inst	Clin, PH			N Lev	N Lev
Cyprus	Ad hoc		MoH*	E(BI), Clin			N Lev	N Lev
Czech Republic				E(BI), Clin			N Lev	N Lev
Denmark	Ad hoc	Formal	NITAG	Clin, PH			N Lev	N Lev
Estonia			NITAG	E(CE), Clin	E(CE)		N Lev	N Lev
Finland	1 or 2/yr		HTAB	E(CE), Clin	E(BI), E(CE)		N Lev	N Lev
France	1 or 2/yr	Formal		E(CE), Clin	Clin		N Lev	N Lev
Germany	1 or 2/yr		NITAG	E(CE), Clin			N Lev	N Lev
Greece			NITAG	Clin	E(BI)		N Lev	N Lev
Hungary			NITAG	E(BI),E(CE),Clin			N Lev	N Lev
Ireland	Ad hoc	Informal	NITAG	Clin, PH	E(BI), E(CE)		N Lev	N Lev
Italy		Informal	MoH*	Clin, PH	E(BI), E(CE)		N Lev, R Lev	R Lev
Latvia			NITAG	Not indicated			N Lev	N Lev
Lithuania			NITAG	E(BI), Clin			N Lev	N Lev
Luxembourg	1 or 2/yr		MoH*	Clin, PH			N Lev	N Lev
Malta	1 or 2/yr		MoH*	E(BI), Clin	E(BI)		N Lev	N Lev
The Netherlands	1 or 2/yr	Formal	MoH*	E(BI), Clin	E(BI)		N Lev	N Lev
Poland		Formal	MoH*	Local epi			N Lev	N Lev
Portugal	Ad hoc	Formal	MoH*	Clin, PH			N Lev	N Lev
Romania			MoH*	Not Applicable				-
Slovakia		Informal		Clin, PH	E(BI)		N Lev	N Lev
Slovenia			MoH*	Clin, PH			N Lev	N Lev
Spain	Ad hoc	Informal	PH Inst	E(BI),E(CE),Clin			N Lev, R Lev	N Lev, R Lev
Sweden	1 or 2/yr	Informal	NITAG	E(CE), Clin	E(CE)		N Lev, R Lev	N Lev, R Lev
United Kingdom	1 or 2/yr	Informal	MoH*	E(CE), Clin				N Lev

Fig. 4. Presence/absence of key steps in the vaccine access pathways of EU28 member states. *Can also be initiated by marketing authorization holder; Green/darker-shaded boxes represent presence of step in the member-state pathway. E(BI), Driver: Economic, budget impact; E(CE), Driver: Economic, cost-effectiveness; Clin, Driver: Clinical; PH, Driver: Public health; Local epi, Local epidemiology; N Lev, National level; R Lev, Regional level; HTAB, health technology assessment body; NITAG, National Immunization Technical Advisory Group; yr, year; MoH, Ministry of Health; PH Inst, Public Health Institution or Commission.

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	

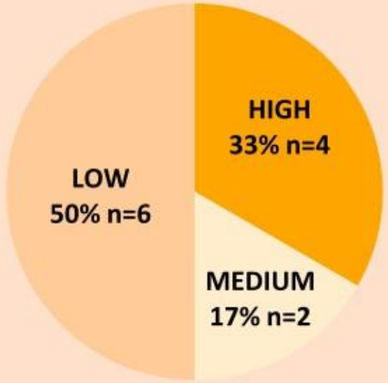
HTAB (n=12) transparency criterion	n	Transparency level
Vaccine-specific decision-analysis framework	3	
GRADE or a similar tool used for the quality of evidence and risk of bias assessment	6	
Recommendations publicly available	8	
Rationale for the decision publicly available	7	

Fig. 5. NITAG and HTAB transparency ratings in the EU28 member states (excluding Romania). Transparency was rated based on the following 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. GRADE, Grading of Recommendations Assessment, Development and Evaluation; HTA, health technology assessment; HTAB, health technology assessment body; NITAG, National Immunization Technical Advisory Group.

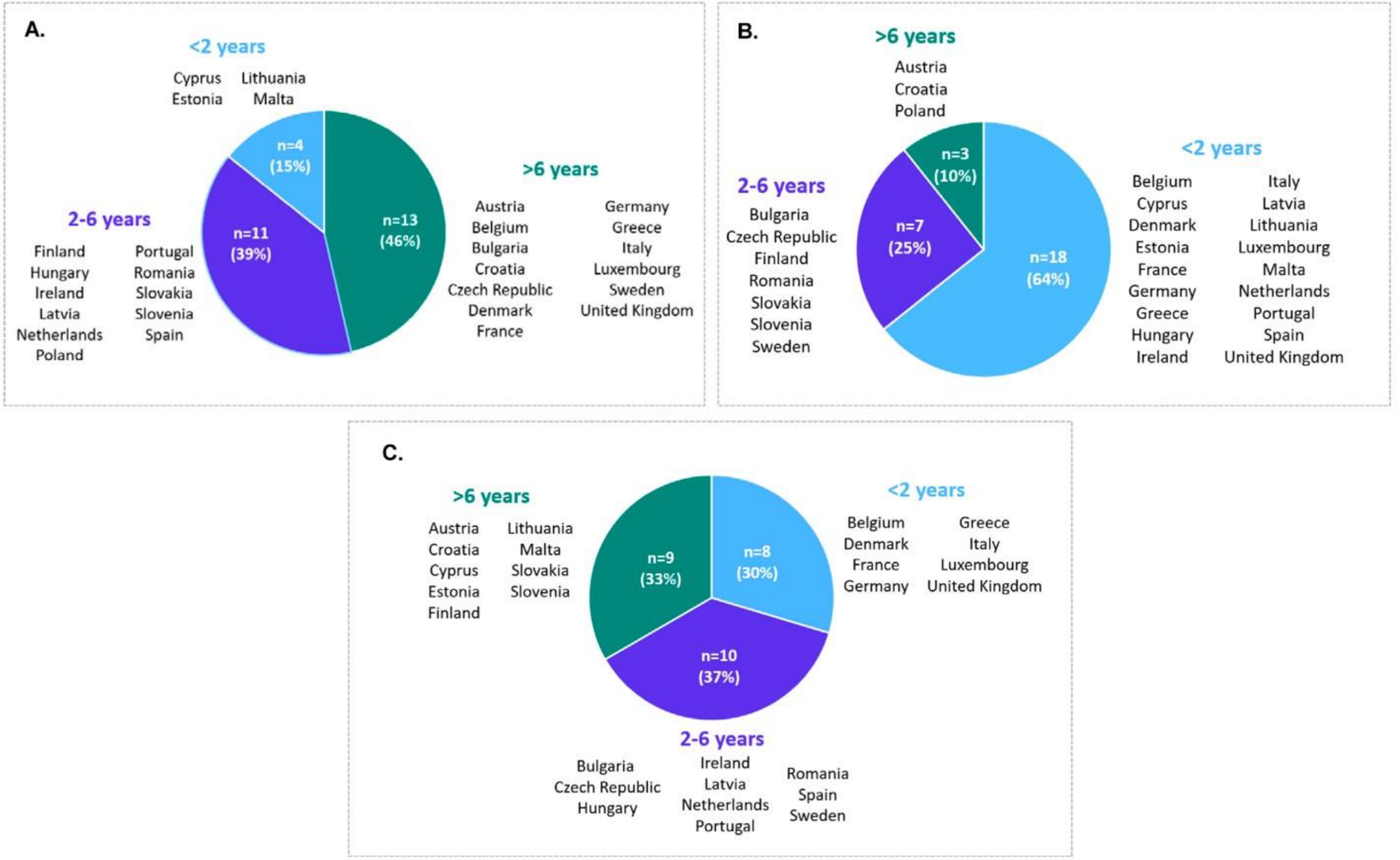


Fig. 6. Estimates of time to population access between the key VMA milestones of: **(a)** marketing authorization to NITAG recommendation; **(b)** NITAG recommendation to funding; **(c)** marketing authorization to population access. TTPA could not be estimated for Poland, as none of the selected vaccines were funded at the time of the research. NITAG, National Immunization Technical Advisory Group; TTPA, time to population access; VMA, vaccine market access.

Table 2
EU28 country clusters based on vaccine market access pathway characteristics.

Cluster 1 **National and regional decision-making + mandatory funding**	**Cluster 2** **National decision-making+ national tendering**	**Cluster 3** **Individual reimbursement**	**Cluster 4** **National decision-making+ mandatory funding (GDP Higher)**	**Cluster 5** **National decision-making + mandatory funding (GDP Lower)**
Countries				
• Belgium[a] • **Italy** • Spain[b] • **Sweden**[b]	• Cyprus • Malta • **UK**[c]	• Czech Republic • **France** • **Germany** • Greece • Slovakia	• Austria[b] • Denmark • Estonia • Finland • Ireland • Luxembourg • **The Netherlands** • Slovenia	• Bulgaria • Croatia • Hungary • Latvia • Lithuania • **Poland**[d] • Portugal • Romania
Shared attributes				
• No formal early advice • Population factor–driven NITAG recommendation • Regional tendering • Published award criteria and clear selection process for tendering	• Horizon scanning in place • No formal early advice	• National level of decision making • NITAG formal terms of reference in place • HTA not binding for respective authorities (if HTA in place; but final decision usually in line with HTA recommendation)	• Public health-driven NITAG recommendation (except Estonia) • NITAG terms of reference (except Ireland) • HTA not binding for respective authorities (if HTA in place; but final decision usually in line with HTA recommendation) • National tendering • Published award criteria and clear selection process for tendering	• No HTA for vaccines (except Bulgaria) • No formal decision analysis framework used by NITAG (except Croatia and Portugal) • Low/medium transparency of decision-making • National tendering • Published award criteria and clear selection process for tendering • Time to access >2 years

Exemplar member states in each cluster are in bold font.
GDP, gross domestic product; HTA, health technology assessment; NITAG, National Immunization Technical Advisory Group.
[a] Recommendation for immunization program issued at national level and recommendation for funding issued at both national and regional levels.
[b] National and subnational tendering.
[c] The UK is the one country in this cluster having truly influential NITAG with formal terms of reference and mandatory (binding) funding at the cost-effective price following inclusion of a vaccine in the immunization program.
[d] Regional level of issuing recommendation on funding also applies but national level of decision-making dominates; mandatory (binding) funding applies only to obligatory vaccination.

Table 3
Drivers and barriers for vaccine access as reported by non-industry vaccine experts in seven exemplar EU member states.

Vaccine access driver or barrier	Exemplar country						
	FR	DE	IT	NK	PL	SW	UK
Drivers							
Burden of disease/actual benefit	■	■	■	■	■	■	■
Vaccine efficacy/effectiveness/safety	■	■	NR	■	■	■	■
Vaccine cost-effectiveness	NR	NR	■	■	■	■	■
Political support	■	NR	■	NR	■	NR	NR
Budget availability/favorable budget impact or price	NR	NR	■	NR	■	■	NR
Availability of registries/experience from other countries	■	■	NR	NR	NR	NR	NR
Barriers							
Budget unavailability	■	■	■	■	■	■	■
Vaccine safety issues or lack of effectiveness	■	NR	NR	■	NR	NR	■
Unclear market access process (e.g., complexity due to the need for a national-regional consensus, or a lack of clarity on process initiation and the role of HTA)	NR	NR	■	NR	■	NR	NR
Organization of vaccination at regional level	NR	NR	■	NR	NR	■	NR
Lack of communication with providers and end-users following vaccination introduction	NR	NR	■	NR	NR	NR	■

Green or red box represents presence of vaccine access driver or barrier, respectively.
FR, France; DE, Germany; HTA, health technology assessment; IT, Italy; NK, the Netherlands; NR, not reported; PL, Poland; SW, Sweden; UK, the United Kingdom.

Table 4
Initiatives or actions to improve VMA*

EU Level
- Improved collaboration to avoid duplication of effort and reduce time to vaccine access for local populations
- Enhanced scientific activities and information sharing (e.g., literature reviews)
- Joint HTA/clinical assessment and development of framework guidelines
- Initiatives to address barriers such as limited research funding and lack of political or health authority support

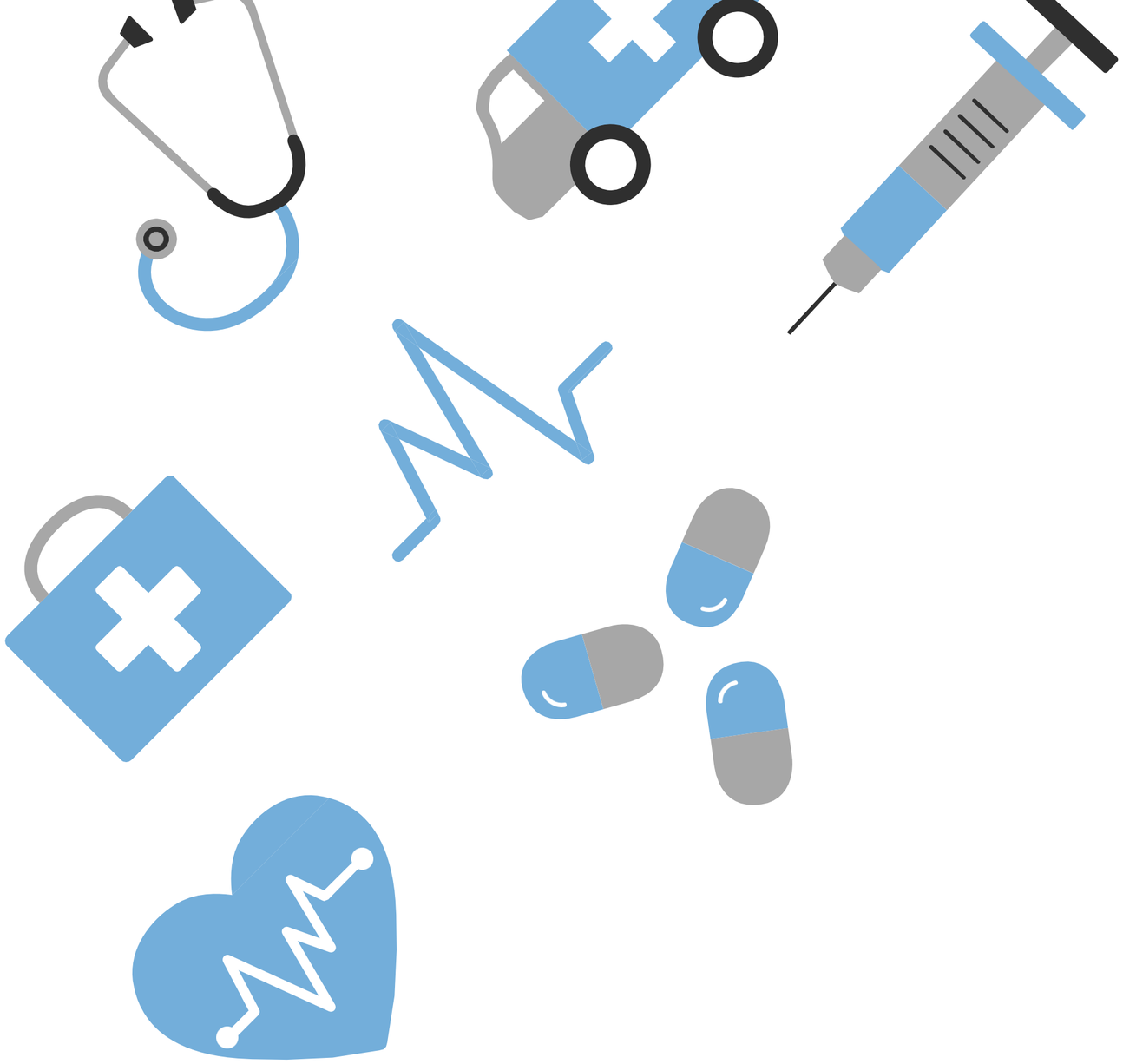
Targeting NITAGs
- Provision of formal early advice
- Input of appropriate vaccine expertise, recognizing that many vaccine experts may be currently excluded from NITAGs due to potential conflicts of interest
- Formalization of horizon scanning, definition of recommendation timelines, and prioritization criteria to select in dossier

Targeting NITAGs and HTABs
- Definition and standardization of NITAG and HTAB roles and decision-making processes
- Greater transparency in assessment and decision-making processes
- Consideration of vaccination demographic effects, equity, country macroeconomic development, and increases in the cost-effectiveness thresholds for vaccines
- Establishment of national public HTABs in charge of independent vaccine evaluations

Targeting vaccine industry/manufacturers
- Early company engagement with vaccine assessment authorities
- Early generation of evidence of vaccine effectiveness
- Securing supply and stocks to avoid delay in the implementation of vaccination programs following the final/local coverage decisions

HTAB, health technology assessment body; NITAG, National Immunization Technical Advisory Group.
* List includes ongoing, partially completed, planned (such as a joint HTA-clinical assessment framework) and new/additional recommendations.

4 Principles for Enhancing Vaccine Assessment and Decision-Making Pathways



Thanks for your attention

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