

## BACKGROUND & OBJECTIVE

- Vaccines market access in European countries (from marketing authorisation to end-user availability) is a long, complex and heterogeneous process.<sup>1</sup>
- Study objective was to objectively classify 28 EU countries into clusters reflecting archetypes of market access pathways for vaccines.

## METHODS

- Description of market access pathway for vaccines was obtained through a primary research among vaccines industry experts in all 28 EU countries and non-industry experts in 5 countries (France, Italy, Poland, the Netherlands and Sweden), and complemented by a comprehensive literature review.
- Hierarchical clustering method was used to classify countries according to selected vaccine market access attributes (Table 1) based on an agglomerative approach (*treating each country as a separate cluster and then merging the clusters until stopping criterion is met*).
  - Jaccard metrics was used to measure the distance between countries (standard method for categorical attributes).
  - Complete-linkage method (considering the distance between the farthest two points from different clusters) was performed. Average-linkage method (considering an average distance from any country of one cluster to any country of another cluster) was used for sensitivity analysis.
  - The optimal number of clusters was selected based on silhouette average width, which describes the distance of each country in one cluster to countries in the neighbouring cluster.
  - To compare the clusters created based on different sets of attributes Adjusted Rand Index (ARI) was used as a measure of cluster similarity.
  - Appropriateness of clusters was checked by Dunn's index (DI) i.e. a ratio between the minimum inter-cluster distances to the maximum intra-cluster diameter (with DI > 1 being a necessary and sufficient condition and higher value indicating better fit<sup>2,3</sup>).
- The results of the clustering were validated by face validity and through discussion with non-industry experts from France, Italy, Poland, the Netherlands and Sweden.

## RESULTS

- Market access pathways for vaccines**
  - The unique feature of the process for vaccines is the recommendation phase performed by the National Immunisation Technical Advisory Groups (NITAGs) in nearly all countries (except Romania).<sup>1,4,5</sup> On top of the assessment conducted by NITAGs, Health Technology Assessment (HTA) is conducted in 12 out of 28 EU countries.<sup>5</sup>
  - Analysed 28 EU countries differ in terms of selected attributes of vaccine market access pathways (Figure 1).<sup>5</sup>
  - The number of vaccinations included in national immunisation program ranges between 5 and 19 in 28 EU countries (Figure 2).<sup>5</sup>

Figure 1. Applicability of key vaccine market access attributes considered for clustering (numbers of EU countries, n=28)<sup>5</sup>

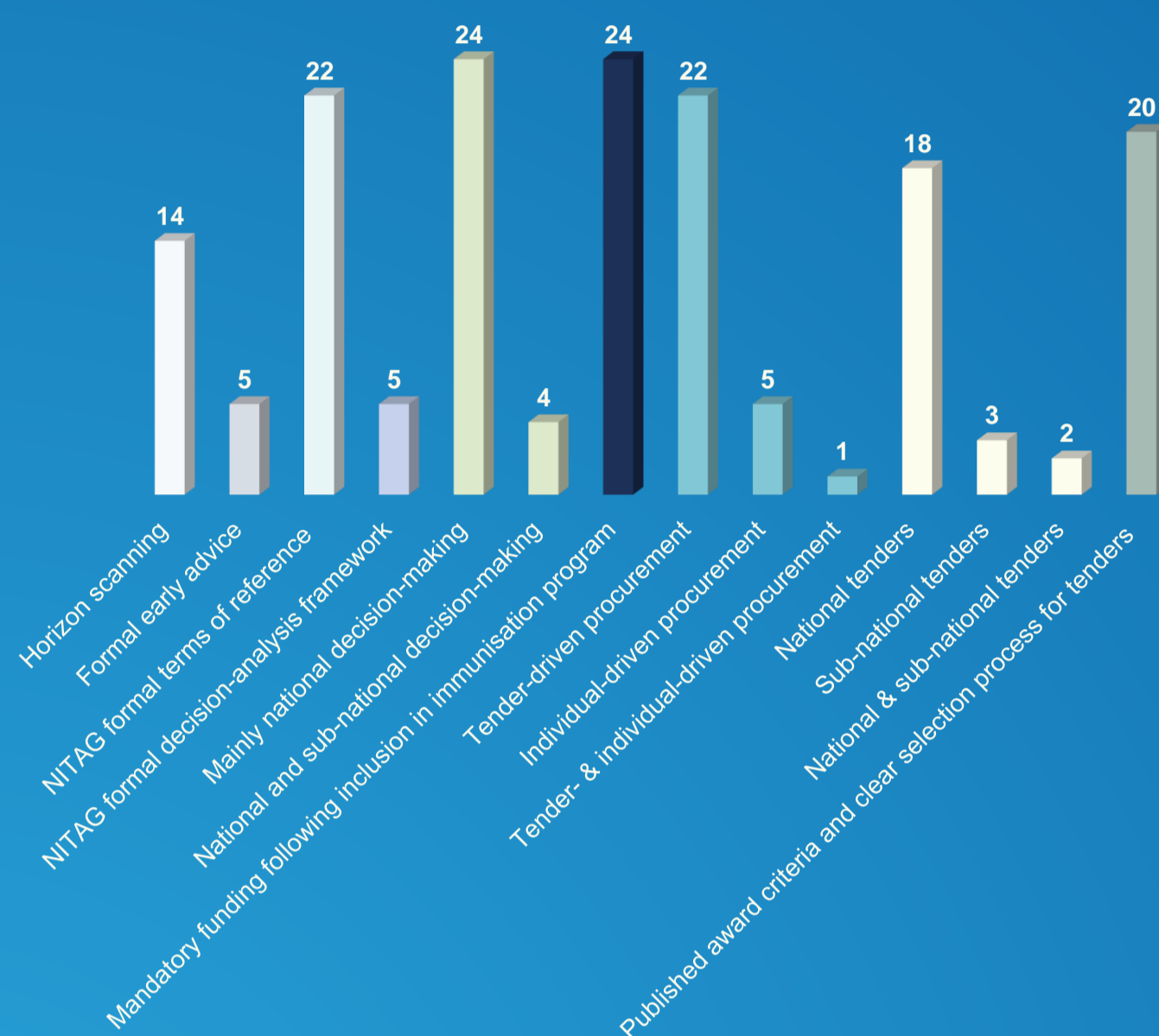
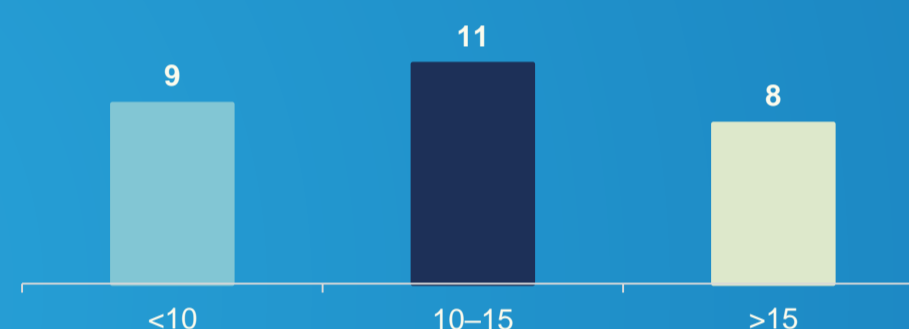


Figure 2. Overall number of vaccinations included in national immunization program (numbers of EU countries)<sup>5</sup>



## Mathematical clustering

- Four clusters were identified through mathematical clustering. However, during face validity the most numerous cluster was split into two separate ones, in order to balance the size of the clusters and to differentiate countries according to their economic status. Implementation of median gross domestic product (GDP) resulted in the final number of five clusters as presented in Figure 3.
- Sensitivity analysis showed that created clusters are stable (countries from each cluster remained grouped together, except Sweden, which was excluded to a separate cluster).
- Irrespective of the clusters the same aspects of vaccine market access were identified as requiring improvement:
  - Generally formal early advice, horizon scanning and NITAG formal decision-analysis framework are not discriminating the clusters because these attributes are lacking in the majority of countries making it impossible to differentiate the clusters.

Table 1. Attributes of the hierarchical clustering

Attributes used for clustering were selected based on primary research on vaccine market access pathways, literature review and statistical parameters*	
1. Applicability of horizon scanning (yes/no)	6. Mandatory funding of at least one vaccine following inclusion of vaccination in immunisation program (yes/no)
2. Availability of formal early advice (yes/no)	7. Procurement type (tender-driven/ individual-driven***/ both)
3. NITAG formal terms of reference (yes/no)	8. Level of tenders (national/ sub-national/ both)
4. NITAG formal decision-analysis framework (yes/no)	9. Published award criteria and clear selection process for tenders (yes/no)
5. Level of decision-making** (national/ sub-national/ both)	10. Number of vaccinations in immunisation program (<10/ 10-15/ >15)
11. GDP implemented during face validity (above/below the median value in the cluster)	

\* Different sets of attributes were tested and finally the set with the best statistical parameters (Silhouette average width, DI and ARI) was chosen.  
 \*\* Issuing recommendation for inclusion into vaccination program and funding  
 \*\*\* Reimbursement list for vaccines

Figure 3. Results of mathematical clustering of 28 EU countries

Typology	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5
	National and sub-national decision-making & mandatory funding	National decision-making without mandatory funding	Individual reimbursement	National decision-making & mandatory funding & higher GDP/capita	National decision-making & mandatory funding & lower GDP/capita
Countries	<ul style="list-style-type: none"> <li>Belgium<sup>1</sup></li> <li>Italy</li> <li>Spain</li> <li>Sweden<sup>2</sup></li> </ul>	<ul style="list-style-type: none"> <li>The UK<sup>3</sup></li> <li>Cyprus</li> <li>Malta</li> </ul>	<ul style="list-style-type: none"> <li>Czech</li> <li>France</li> <li>Germany</li> <li>Greece</li> <li>Slovakia</li> </ul>	<ul style="list-style-type: none"> <li>Austria<sup>2</sup></li> <li>Denmark</li> <li>Estonia</li> <li>Finland</li> <li>Ireland</li> <li>Luxembourg</li> <li>The Netherlands</li> <li>Slovenia</li> </ul>	<ul style="list-style-type: none"> <li>Bulgaria</li> <li>Croatia</li> <li>Hungary</li> <li>Latvia</li> <li>Lithuania</li> <li>Poland<sup>4</sup></li> <li>Portugal</li> <li>Romania</li> </ul>
Homogeneous attributes	<ul style="list-style-type: none"> <li>No formal early advice for vaccines</li> <li>Population-based aspects driving NITAG recommendation</li> <li>Sub-national tendering</li> <li>Published award criteria and clear selection process for tendering</li> </ul>	<ul style="list-style-type: none"> <li>Horizon scanning for vaccines in place</li> <li>No formal early advice for vaccines</li> <li>National tendering</li> </ul>	<ul style="list-style-type: none"> <li>National level of decision-making</li> <li>NITAG formal terms of reference in place</li> <li>HTA not binding for respective authorities (if HTA in place; although the final decision usually in line with the recommendation)</li> </ul>	<ul style="list-style-type: none"> <li>Population-based aspects driving NITAG recommendation (except Estonia)</li> <li>NITAG terms of reference in place (except Ireland)</li> <li>HTA not binding for respective authorities (if HTA in place; although the final decision usually in line with the recommendation)</li> <li>National tendering</li> <li>Published award criteria and clear selection process for tendering</li> </ul>	<ul style="list-style-type: none"> <li>No HTA for vaccines (except Bulgaria)</li> <li>No formal decision analysis framework used by NITAG (except Portugal)</li> <li>Low/medium transparency of decision-making</li> <li>National tendering</li> <li>Published award criteria and clear selection process for tendering</li> <li>Time to access &gt;2 years</li> </ul>

<sup>1</sup> National level of issuing recommendation for immunisation program & both (national & sub-national) levels for issuing recommendation for funding  
<sup>2</sup> National and sub-national tendering  
<sup>3</sup> The UK is the one country in this cluster having truly influential NITAG with formal terms of reference; A vaccine will be obligatorily funded only if requested by Secretary of State, issued by the Joint Committee on Vaccination and Immunisation and in case of demonstrated cost-effectiveness.  
<sup>4</sup> Sub-national level of issuing recommendation on funding also applies but national level of decision-making dominates; Mandatory funding applies only to obligatory vaccination.

## REFERENCES

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## CONCLUSIONS

- Mathematical clustering allowed to objectively identify 5 archetypes of market access pathways for vaccines among the EU28 countries.
- Countries within the same cluster are more similar to each other than to countries in other clusters, based on the considered criteria.
- Clustering can provide unique insights into key areas for improvement of vaccines market access beyond the individual country level.
- While some key areas for improvement might apply to all EU28 countries, the country archetypes show that for other key areas a one-fits-all EU28 policy approach might be limited.