Vaccine ecosystem health check: Identifying the components and experiencing the complexities

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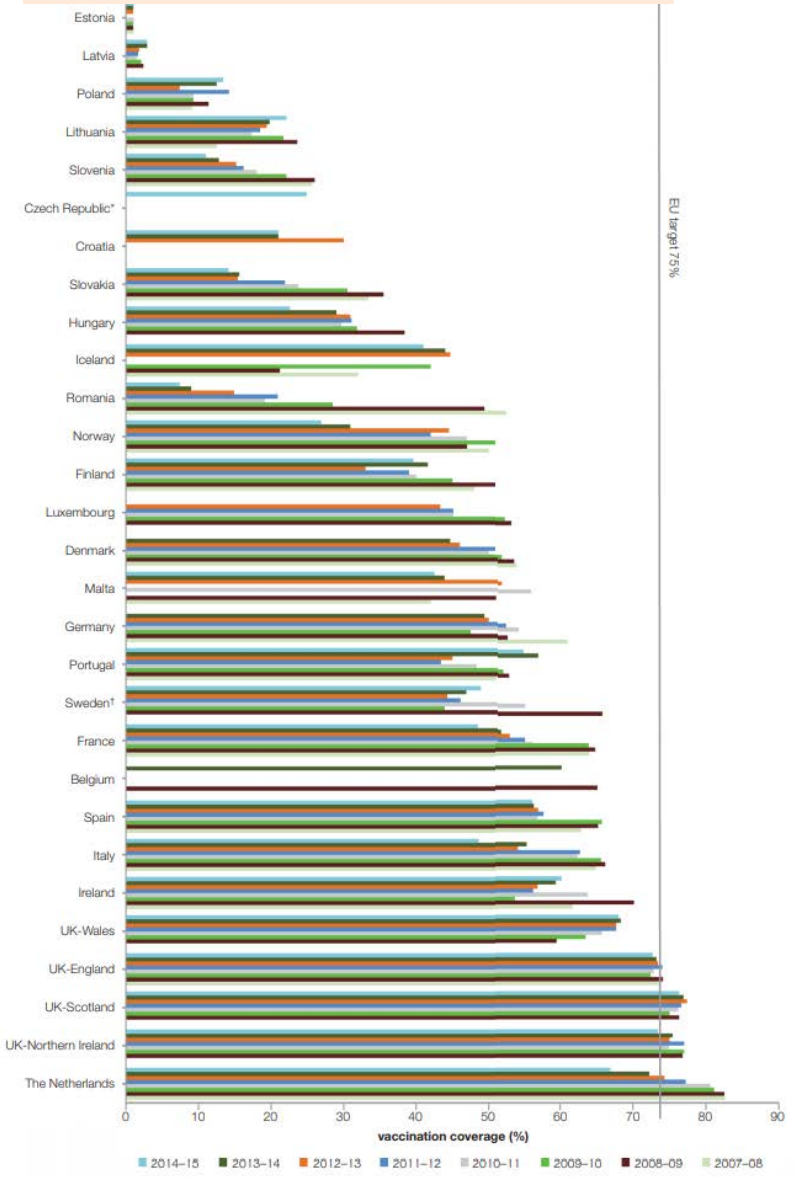
Outline

- Background: Vaccines and medicines; vaccines development process
- Vaccines ecosystem: General features
- Vaccine policies in Europe
- Key issues and possible solutions
- National plans and international partnerships
- Conclusions

Background

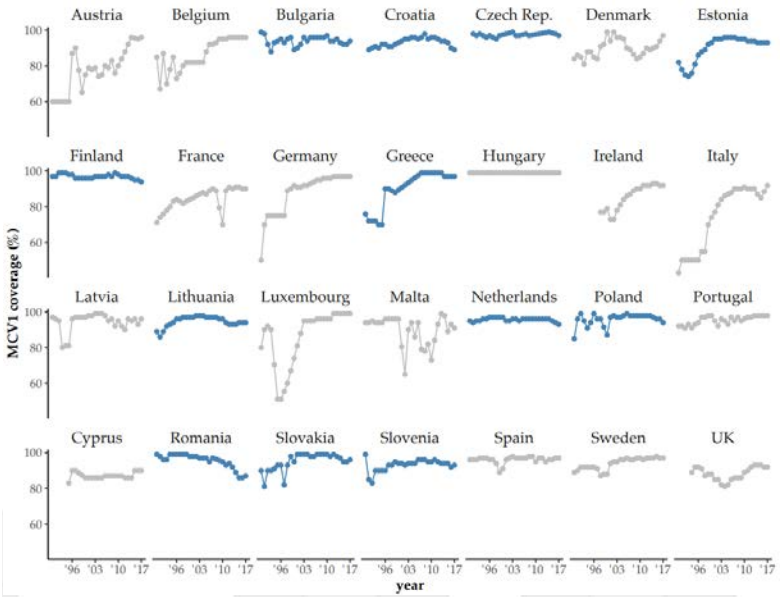
Seasonal influenza vaccination coverage



- **Vaccination** is among the mainstays of prevention and represent one of the most cost-effective ways of avoiding infectious disease
- Globally prevents at least 2-3 million deaths a year and with improvements in the coverage it could avoid further 1.5 deaths per year [1]

Despite this there is a **decline** in the uptake of key vaccines, particularly in children

Insufficient vaccination coverage, outbreaks of vaccine-preventable diseases, particularly measles



Resilient immunization programmes strongly contribute to sustainability of health care systems

1. European Commission, World Health Organization – Global Vaccination Summit, September 2019
Table on the left: Seasonal influenza vaccination coverage rates in older age groups.
Source: European Commission, The organization and delivery of vaccination services in the EU
Table above: Measles coverage in EU member states.
Source: European Commission – State of vaccine confidence in the EU 2018

Background: Vaccines and medicines

- Vaccines are defined as “products that stimulate a person’s immune system to produce immunity to a specific disease, protecting the person from that disease”

While

- Pharmaceuticals are chemical, herbal or biological products used for diagnosis, cure, mitigation, treatment, or prevention of disease intended to affect the structure or any function of the body of man or other animals

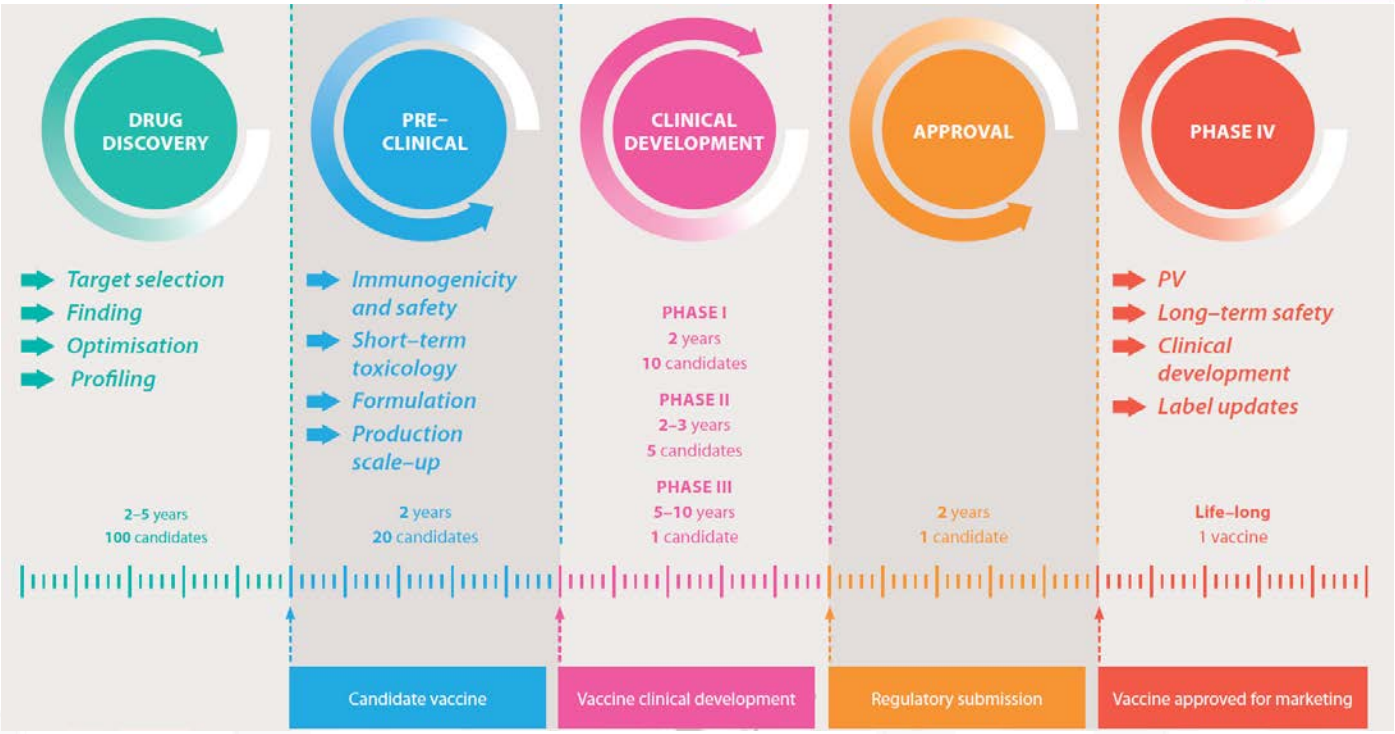
The vaccines market is, compared to the pharmaceuticals market:

- Smaller and concentrated on both the demand- and the supply-side, since it is composed of individual markets for each vaccine or vaccine group, each one carrying its own complexities. This is more marked on the supply-side[1]
- (Equally) highly regulated due to complex quality and safety concerns and new technical issues arising from a necessary increase in the speed of innovation
- Highly dependent on public and charitable investors, specially for low and middle income countries

1. World Health Organization – Vaccine Market. Available online at: https://www.who.int/immunization/programmes_systems/procurement/market/en/

Overview of the development of vaccines

- Three major factors are contributing to these timelines: Safety, quality and efficacy controls, data collection from different countries, different regulatory requirements
- Marketing authorisation of vaccines in EU can be done through three pathways:



1. Centralised procedure, where the evaluation is done by the Committee for Medicinal Products for Human Use (CHMP);
2. Mutual Recognition Procedure (MRP), where a reference member state evaluates and approves the product and after is recognised by other European Countries or
3. National Procedures, this pathway is viable only for products licensed in one specific country

- In US the regulatory evaluation of vaccines is reviewed by the Centre for Biologic Evaluation and Research (CBER) which oversees and regulates therapeutic and prophylactic vaccines eithin the safety, quality and effectiveness standards set by the FDA. FDA is also responsible for the review and authorization of clinical trials, approval of licensing application, lot release and monitoring the performance of the product throghout its life cycle[1]

1. Baylor N. W. – Role of the national regulatory authority for vaccines. 2017

Vaccine uptake decline: Reasons?

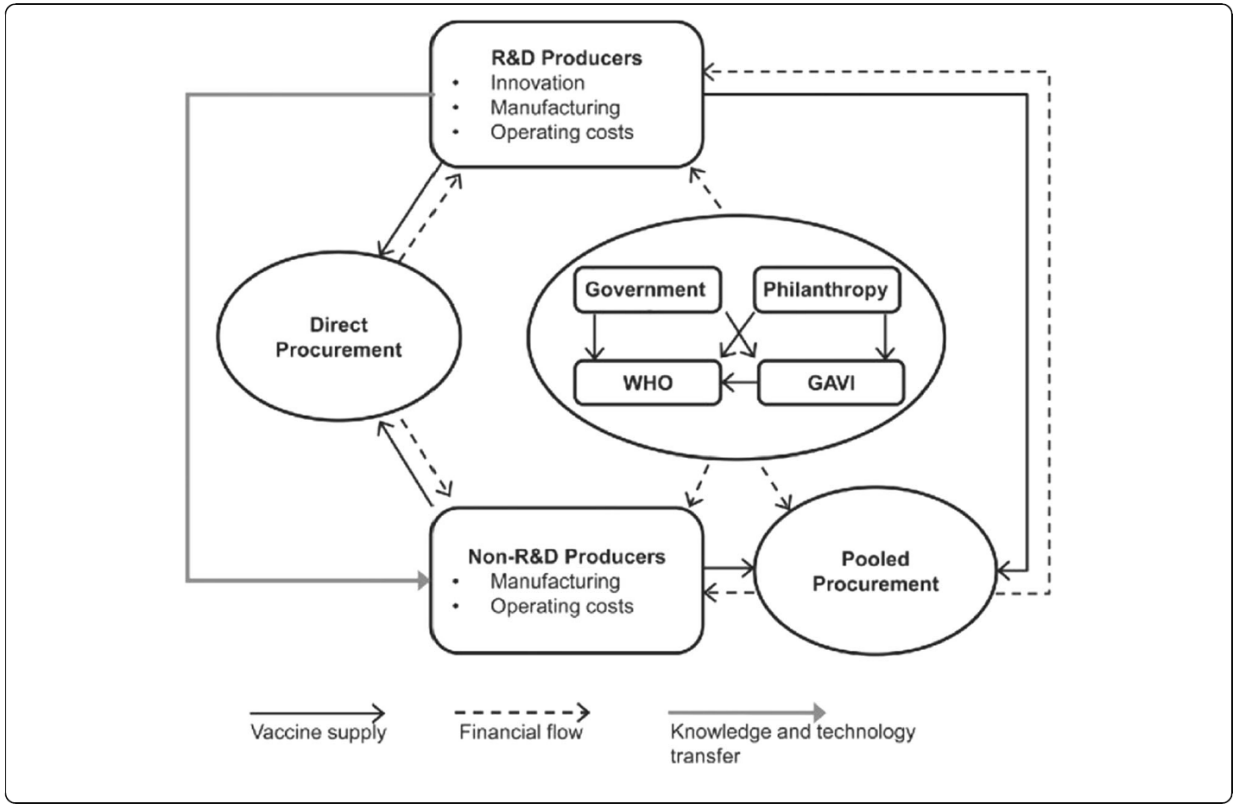
According to the recent Global Vaccination Summit, this trend may be caused mainly by:

- **Vaccine hesitancy**, i.e. delay in acceptance or refusal of vaccination despite availability of vaccination services[1]
- **Lack of patient confidence**, namely patient distrusts the efficacy and safety of vaccines. This is strictly related to the next point
- **Misinformation** about vaccines risks and benefits, due to wrong information about vaccines features
- **Logistical and practical factors**, e.g. distance from medical practice or hospital
- WHO has listed vaccine hesitance as one of the ten threats to global health in 20191

1. European Commission, World Health Organization – Global Vaccination Summit, September 2019

Vaccine ecosystem: a simplified model

- The vaccine ecosystem is multilayer in essence, where decision-making has impact at global, regional and national level
- Vaccine producers can be distinguished in two groups, according to how they invest their revenues: R&D investors and those who invest on manufacturing and sales
- R&D investors are generally multinational firms based in US and Europe



- Governments, philanthropic organizations, WHO, GAVI are the main vaccine purchasers
- UNICEF is the global lead for vaccine procurement
- Continuous changes in supply and demand explain a dynamically evolving market

Elahi M.S. et al – Vaccination ecosystem health check: achieving impact today and sustainability for tomorrow

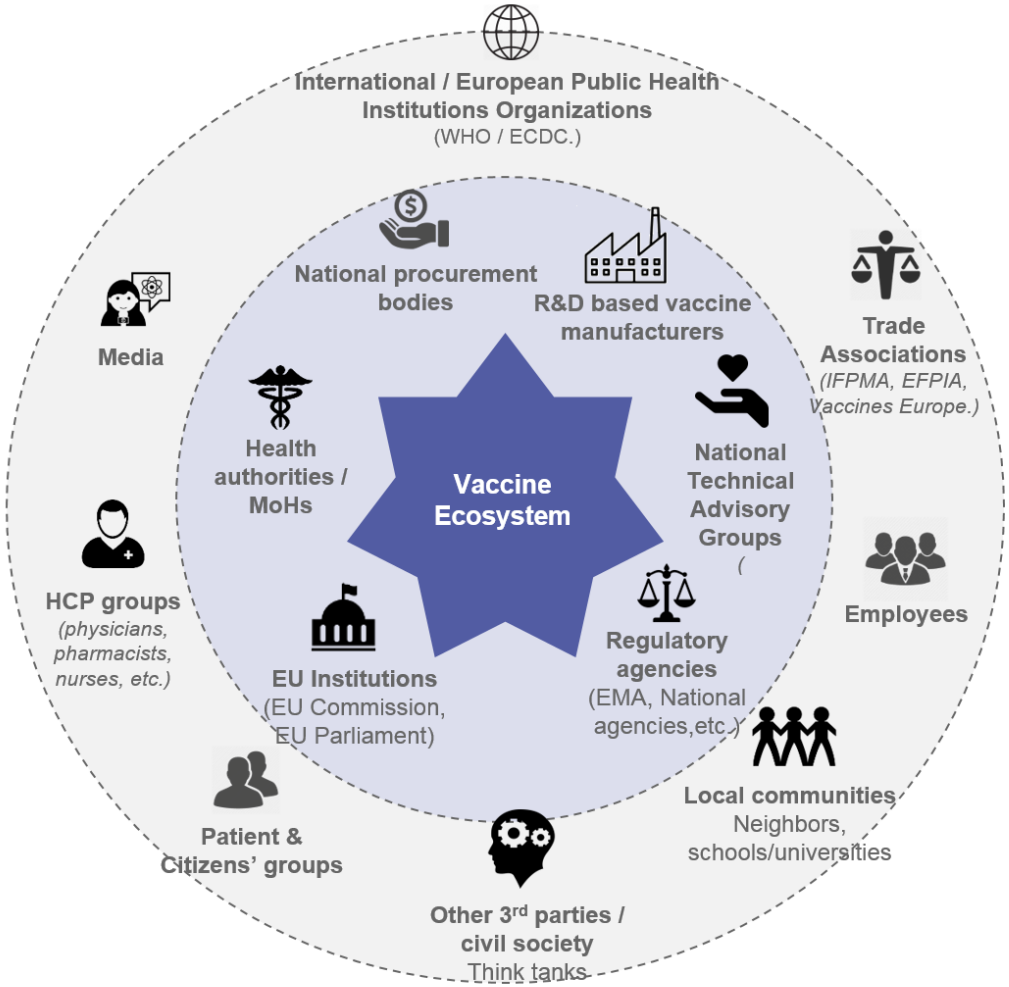
Vaccine ecosystem interdependencies

Vaccine Ecosystem Interdependancies chart

Stakeholders are interdependent in the ecosystem; even a specific decision might have a relevant impact on the sustainability of the ecosystem as a whole

The interdependancies chart shows how at the centre of the ecosystem there are regulators, European institutions and vaccine manufacturers, while outside the main group there are intermediate bodies (i.e. trade associations, healthcare providers groups, local communities, patient and citizens' groups, civil society), Intergovernmental institutions (WHO and ECDC) and media.

This framework includes a large variety of stakeholders which makes the ecosystem a complex space where different interests, goals and decisions are made



Vaccine policies in Europe

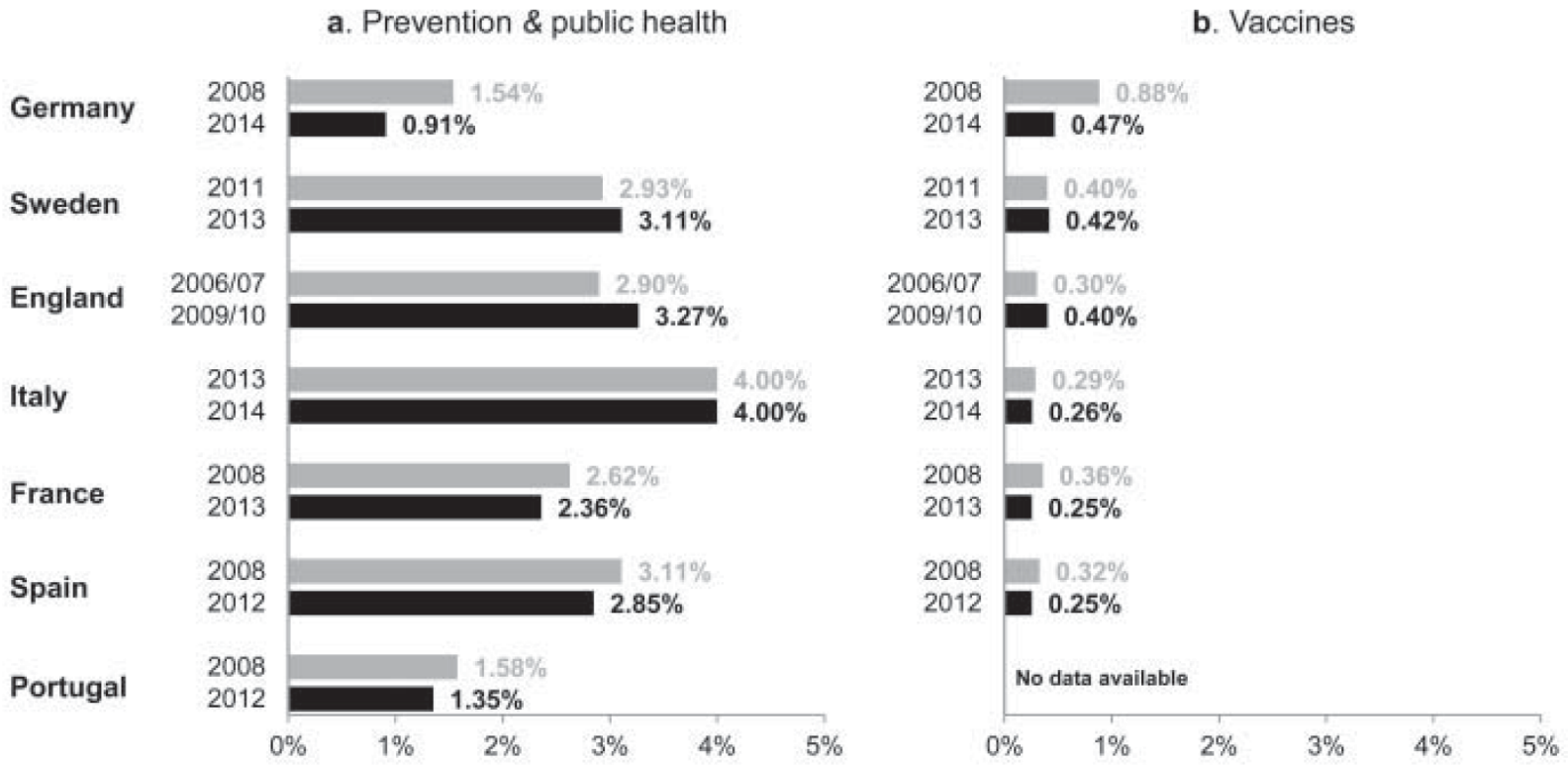
- Vaccine policies in Europe are a national competence, where we find on a country level Ministries of Health, public health institutes, procurement agencies, payers and regulators.
- EU institutions manage the marketing authorisation process
- At EU-level, we have best practice sharing and recommendations, while there are efforts for better harmonisation.
  - The Council adopted in December 2018 a Recommendation to strengthen the EU cooperation on vaccine-preventable diseases.
  - The initiative aims to tackle vaccine hesitancy, improve coordination on vaccine procurement, support research and innovation, and strengthen EU cooperation on vaccine-preventable diseases
- The EU market is of course impacted by the global status and the market dynamics beyond the European borders; this all adds up to the complexity.

European Union market fragmentation:

- Member States have competence on health policy, which impacts vaccination programmes, infrastructure, access and population protection
- However, infectious diseases do not stop at national borders. Recent measles outbreaks are the perfect example: According to the World Health Organization (WHO), in 2018, 353,236 measles cases were reported globally; 23% (82,523 cases) of these cases were reported from countries in the European region
- Between 1 January 2016 and 31 March 2019, 84 deaths caused by measles cases were reported for the EU/EEA countries alone[1]

European Commission, World Health Organization – Global Vaccination Summit, September 2019

Vaccine spending in select European countries

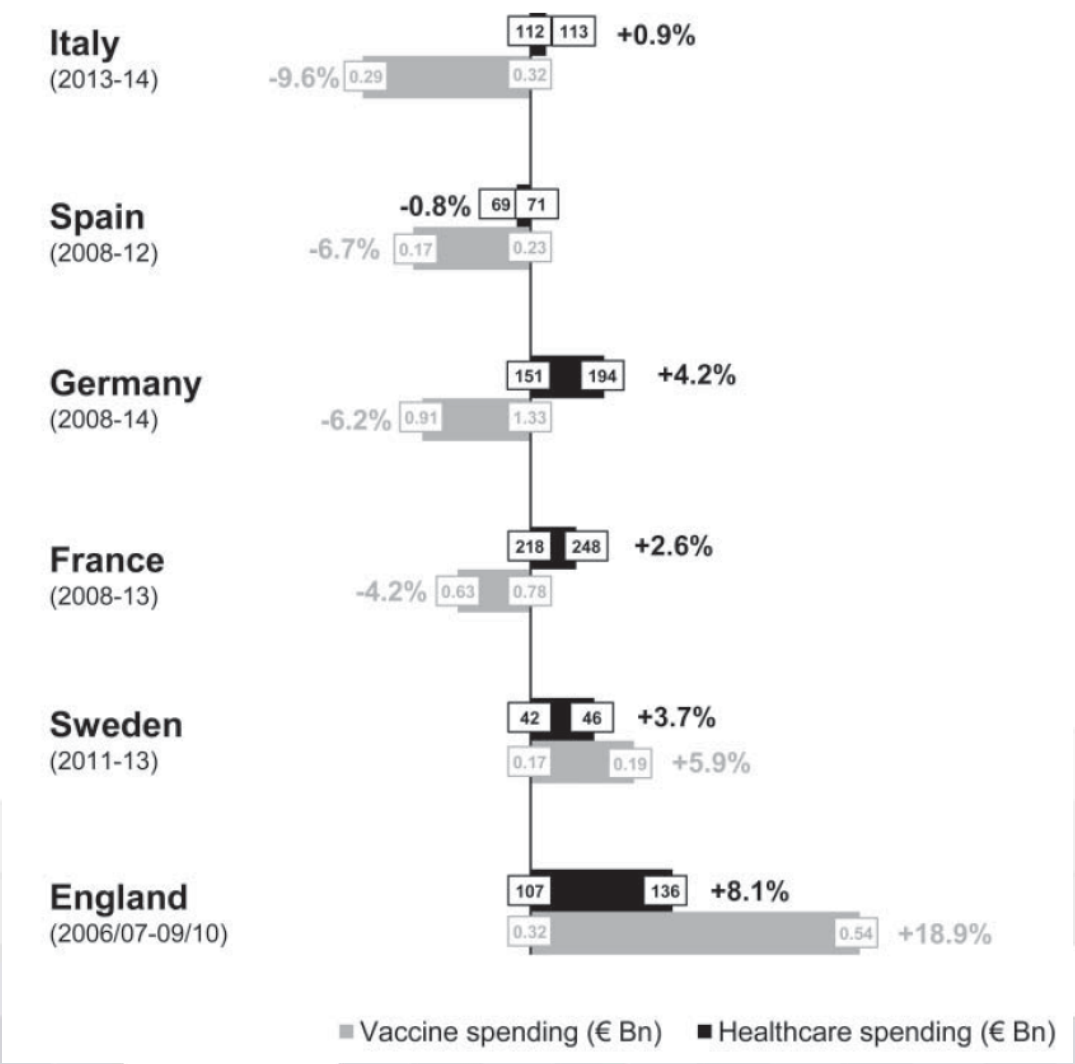


Proportion of national healthcare spending devoted to prevention and vaccines:

- Western European countries spend no more than 0.5% of their healthcare budgets on vaccines
- Vaccine expenditure ranges from 0.47% in Germany to 0.25% in Spain and France
- Vaccines procurement budget are proportionally decreasing in respect of national healthcare budgets

Ethghen O. et al – How much money is spent on vaccines across Western European countries?

Healthcare and vaccine spending evolution in select European countries



- All countries considered with the exception of Spain increased their healthcare spending
- Healthcare spending increase range from 0.9% in Italy to 8.1% in England
- Vaccine spending decrease range from -9.6% in Italy to -4.2% in Sweden
- Sweden and England increased vaccine spending in the periods considered
- Prevention and vaccination represent a small part of the healthcare spending in Western Europe, falling respectively below 5% and 0.5%

Ethgen O. et al – How much money is spent on vaccines across Western European countries?

What are the key issues for a “healthy” vaccines ecosystem?

- Healthy markets supply the right quantities of goods and/or services to the right people at the right price

Current key issues for a healthy vaccines market are:

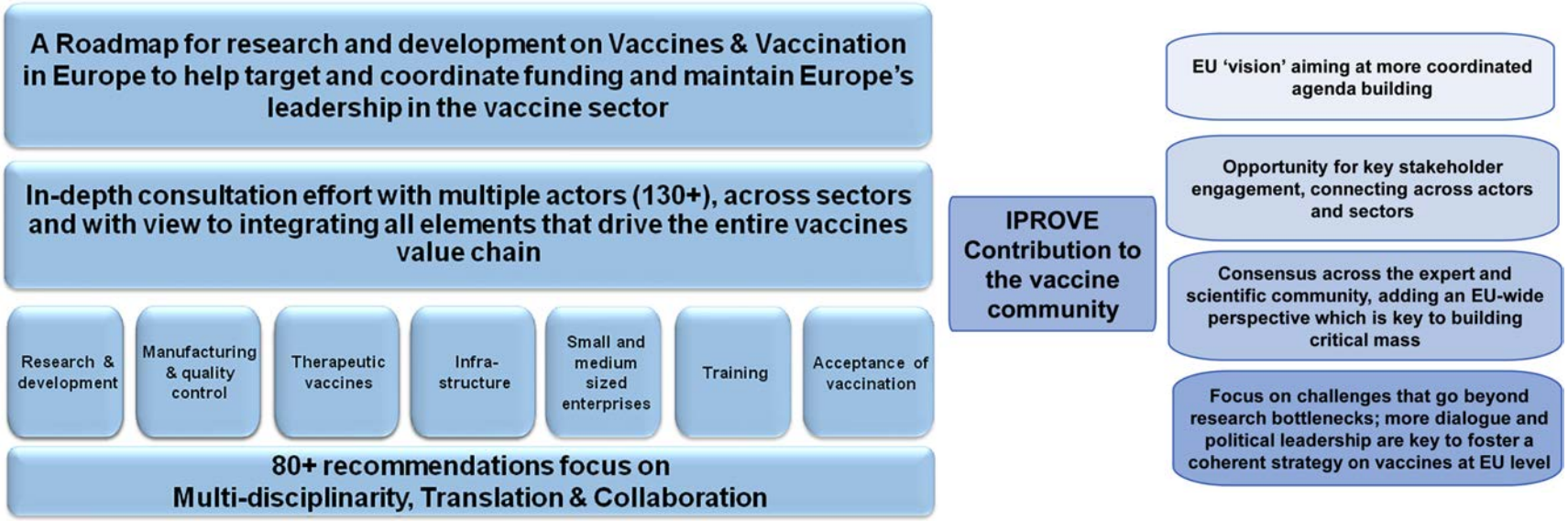
- **Asymmetries**: Supply/distribution and cost/profitability asymmetries, due to few research-driven companies and small and decreasing numbers of suppliers & manufacturing facilities
- **Gaps**: between programmes like the WHO global vaccine action plan (GVAP)/ Global Immunization Vision and Strategy (GIVS) and market shaping (due to “price reduction” metrics and underdeveloped metrics for future innovation and supply security
- **Population growth:** particularly in low and middle income countries where vaccine procurement and manufacturing is often lacking
- **Wider targeting**: Increase in the number, doses and cost of vaccines targeting a wider age group beyond that of infants
- **Vaccine supply and price**: influence the availability, financing, pricing and procurement
- **Inadequate systems and innovation issues:** due to technological and programmatic issues (i.e. supply chain, cold chain custody, health care worker education, i.e. capacity for manufacturers, especially in LMICs, to efficiently organize the supply chain and train the involved workers)

Key issues for a healthy vaccines ecosystem: possible solutions

Some potential solutions can be:

- **Guaranteed return on investment** for donors, governments and global stakeholders, to improve the investments and reduce the risks. Policy-makers and intergovernmental organization could address this issue through regulation or/and better management
- **Presence of multiple effective suppliers** to reduce local/regional monopolies and secure supply, since the number of manufacturers is decreasing, with implications on prices and procurement
- **Financing for R&D**, to enhance research on vaccines and develop the market of vaccines
- **Political prioritization** by raising awareness about needs, i.e. fighting anti-vaccines rhetoric and developing outreach programmes
- **Empowerment of developing country manufacturers** (e.g. technology transfer), so as to help countries that are not producing vaccines to create a favourable environment for new manufacturing companies/facilities
- **Balance of public-private perspectives** for public goods and distinction of the roles of each sector, i.e. by improving national and international legislation in order to avoid distortions in the market

The case of IPROVE roadmap



- The IPROVE (Innovation Partnership for a Roadmap on Vaccines in Europe) FP7 project was conceived to propose a roadmap for European investment in innovative science and technology for vaccines
- IPROVE gathered more than 130 public and private stakeholders from academia, government, industry and small enterprises to develop a virtuous roadmap for investments in Europe
- More than 80 recommendations produced, mainly on how to stimulate innovation and fostering real collaboration within the European vaccine ecosystem
- IPROVE represent a first attempt to develop a comprehensive view of the European vaccine ecosystem

Medaglini D. et al – Innovation Partnership for a Roadmap on Vaccines in Europe (IPROVE): A vision for the vaccines of tomorrow

Conclusion

- Resilient immunization programmes strongly contribute to sustainability of health care systems
- As health care systems need to improve performance and allocate resources more efficiently, national vaccination programmes have a key role to play in this
- Vaccine ecosystem represents a particular and complex environment of a healthcare market where its regulation, supply- and demand-side patterns and policy proposals differ from the general pharmaceutical framework
- Responding to the challenges imposed on vaccine markets (population growth and dynamics, vaccine hesitancy, regulatory burden, among others), requires coordinated effort
- Such effort, could mean in Europe, the creation of a regional platform where all relevant stakeholders can interact; this way
    - Best practices can be developed on investment, regulation and evidence-based approaches
    - Drawbacks & existing silos can be mitigated and, ultimately, overcome